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The Third Inter-American Cardiological Congress

The Third Congress was held in Chicago, June 13-17, 1948, under the auspices of the Inter-American Society of Cardiology and the National Heart Associations of the Western Hemisphere. Its sponsors were the American Heart Association, the Chicago Heart Association, and the Illinois Heart Association. The host institution was Michael Reese Hospital. Members and official delegates came from thirty-six countries. At the inaugural session, they were officially welcomed by the Hon. Oscar R. Ewing, Federal Security Administrator and personal representative of the President of the United States; by Dr. Roland Cross, Director of the Illinois Department of Public Health and personal representative of the Governor of the State of Illinois; by Dr. Herman Bundesen, President of the Chicago Board of Health and personal representative of the Mayor of the City of Chicago; by Dr. Arlie R. Barnes, President of the American Heart Association; by Dr. George K. Fenn, President of the Chicago Heart Association; by Dr. Harry A. Durkin, President of the Illinois Heart Association; by Mr. Grant Pick, President of the Michael Reese Hospital; and by the President of the Congress. Greetings extended on behalf of the delegates are included. Through the leadership and untiring efforts of its local committees and its officers, particularly its President, Dr. Louis N. Katz, the Congress was completely successful.

In recognition of the success and significance of this fine cooperative effort, which already is exercising an international influence, this issue of the American Heart Journal is being devoted to the business, social, and scientific proceedings of the Congress.

EXCERPTS FROM BUSINESS AND SOCIAL PROCEEDINGS

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GREETINGS FROM MEXICO EXTENDED BY DR. IGNACIO CHÁVEZ AT THE INAUGURAL SESSION

ONCE more those who study and practice cardiology have the pleasure of meeting together in this Continent. When the first Inter-American Congress was held in Mexico in 1944, its members included only a few Mexican cardiologists and a small group of our friends in the United States, Cuba, and Central America. However, our call was answered by some of the world's leading scientists, and sponsored by them, the Inter-American Society of Cardiology was born.

When we held the Second Congress about two years ago, we were not a small gathering but a magnificent and important group which included representatives of all of the cardiology societies on the American Continent and a select number of European cardiologists, who were the especially invited guests of Mexico. The International Council of Cardiology was established under its auspices; it will soon issue a call to cardiologists all over the world to meet in Europe in 1950.

As we celebrate our third reunion, it is a pleasure to review the ever increasing importance of our successive meetings. To the Heart Associations of Argentina, Brazil, Cuba, the United States, and Mexico, which took part in the last Congress, we have now added the recently organized Societies of Canada and Peru. We are grateful also for the increasing interest and enthusiasm displayed by our English-speaking colleagues, as evidenced by their support and by their

contributions to this Congress. Finally, we rejoice in having with us representatives from European Societies of Cardiology, as well as from the old universities of Europe. We men of science of the New World salute and extend fraternal greetings to our illustrious European colleagues who are with us.

The success of this Congress is already assured. Under the wise leadership of Dr. Katz and with the support given us by the outstanding sponsors, this Congress will surely mark an epoch in the development of our specialty. Its success should not be measured only in terms of the number of participants, which is larger than ever, nor by the importance of their contributions, which is indeed great. These yardsticks, important though th[redacted]ot fully measure the significance of this Congress. Behind it all th[redacted]piritual meaning; something which is as valuable in human relations [redacted]nces achieved in the scientific field. This spiritual value leads to mu[redacted]tanding between individuals and whole nations; it does away with th[redacted]olationism and reinforces the bonds of mutual respect and friendship.

We are physicians and as such we are primarily concerned with the advances of medicine, but we are also members of the human race, and, furthermore, citizens of various countries which we love and honor. Pasteur has said, "Science knows no boundaries but the scientist has a fatherland." Therefore, each of us wishes to bring to his country well-earned prestige, respect, and honor.

This Congress offers the best opportunity to achieve these aims. We have brought here the best product of our efforts. Humble or rich, it constitutes a fine harvest which is dedicated to mankind's welfare. Fortunately, medicine is perhaps the only science whose objectives have not been perverted; the accomplishments of its investigators have not been turned into a means of destroying humanity.

The great city of Chicago had been selected to be our host because we realize the value of its contributions to the advance of medicine in the United States. If it were not for the splendid research work which is being done by the members of the Chicago Heart Association, the unique past contributions of Herrick and the present notable contributions of Katz would suffice to make Chicago the outstanding cardiac center that it is. Here, during this week, we shall witness the depth and richness of this country's scientific life as reflected by Chicago's medical institutions.

Fellow members: In the name of the Mexican delegation, I wish to thank the Michael Reese Hospital and its affiliated institutions for the generous hospitality accorded us. We pray for the success of this Congress and for mutual understanding between our countries through their men of science.

GREETINGS FROM ARGENTINA EXTENDED BY DR. PEDRO COSSIO AT THE INAUGURAL SESSION

IT IS an honor which far exceeds any merit of mine that I should have been chosen by the Directive Committee of the Third Inter-American Cardiological Congress to deliver a speech at this Inaugural Session and to represent South American cardiology, which is one of the oldest offshoots of the specialty of cardiology of this great and beautiful sister country.

In South America, cardiology made a somewhat precocious start as a specialized school of medical science in the first quarter of the present century; its pioneers were Raphael Bullrich and Gregorio Martinez of Argentina, Oswaldo de Oliveira of Brazil, and Julio Montes Pareja of Uruguay. Their inspiration emanated from the French School because directly or indirectly they were pupils of Henri Vaquex, who paid us a visit in 1924, and brought us up to date on the advantages of the use of ouabain in the treatment of heart failure.

The discoveries with regard to the mechanism of cardiac rhythm performed by Carl Wenckebach of Vienna and Sir James Mackenzie in conjunction with

Sir Thomas Lewis of London caused South American cardiology to turn its attention to these other Schools, and finally and definitely to align itself with that of the United States, when James B. Herrick of Chicago and Harold E. B. Pardee of New York established the clinical and electrocardiographic diagnosis of myocardial infarction.

Another important factor which guided South American cardiology toward its present course were the books, now classics, on diseases of the heart by Paul D. White and Samuel A. Levine. Both of these books had to be translated into Spanish to satisfy an insistent demand.

More important than all this, however, was the visit to South America in 1942 of Frank N. Wilson. Not only did he teach us, morning, noon, and night, everything necessary for the practice of rational and not merely empirical electrocardiography, but he succeeded in imparting his ideas and awakening a spirit of real investigation of the unknown; that is to say, he created a school of thought, with the result that we all esteem and venerate him as a veritable master mind.

The final link in the drawing together of the cardiological schools of North and South America was supplied by the Argentine Society of Cardiology, when it translated and adopted for the diagnosis of diseases of the heart the criteria and nomenclature prepared by the New York Heart Association, which had already been adopted by the American Heart Association. This action signifies that today throughout the whole of America the language of cardiology is one and the same, facilitating its comprehension and knowledge.

To finish with this brief summary, I wish to remember the names of the two forerunners. One was Francisco de Castro of Brazil, who published a noteworthy book in 1895 on the circulatory system, with profuse quotations from English and German literature, which at that time was almost unknown in South America. The other was Bernardo Houssay, an Argentine, who in 1930 sent one of his pupils to Western Reserve University to study the recording of cardiac sounds with Carl J. Wiggers, with the result that ever since then, Buenos Aires has made the greatest contribution toward the solution of this problem.

The natural consequence of all this is that the literature of cardiology which has held the first place during the last twenty years is that of this marvelous country. The desire to come here to study in your medical institutions becomes more fervent and widespread every day.

I myself came here for that purpose in 1936 and came back again in the year 1942 to deliver the Lewis Conner Lecture at the 18th Annual Scientific Meeting of the American Heart Association. Now I am here for the third time in my role of delegate to the Third Inter-American Cardiological Congress, that magnificent project of Ignacio Chávez of Mexico, which on the present occasion has been converted into a reality by Louis N. Katz, our present President.

The first time I took back with me to South America the knowledge I had acquired of something new, especially regarding methods of work. The second time I came here with my own humble personal experiences. Now I am the bearer of a message from the whole of South America to ask that the next Inter-American Cardiological Congress be held there. I trust that you will see fit to accept this invitation. In any event, I wish to express my thanks, no matter what the decision may be.

GREETINGS FROM EUROPE EXTENDED BY DR. GUSTAV NYLIN OF STOCKHOLM, SWEDEN, AT THE INAUGURAL SESSION

WITH the decline of the Greek civilization, the glorious heritage of Greek culture, art, and science passed to the younger, more vigorous Roman Empire. It was not merely that prominent Greek scientists and artists emigrated. It was rather that the sciences were reborn in the young Roman Empire and underwent unparalleled development. This new knowledge was later trans-

planted to France, and from there to the rest of the civilized world. The comparison is obvious when I, as a European physician, feel it a great privilege and pleasure to come to the American continent, which today is the foremost center of a tremendous expansion in culture and science. As a native of Sweden, I quite naturally see tangible proof of this in the fact that not less than 50 per cent of the Nobel Prize awards have been made to Americans in the years 1938 through 1947.

Cardiology as a field of research, like the cardiological associations, is of relatively recent origin, and the United States has played a major part in its development. But, though cardiology in its present form is a comparatively young science, the history of the study of the heart reaches back into antiquity. I need only mention how the heart was used as a symbol by the Egyptians and many other peoples, how it captured the imagination of primitive tribes, and how, through the centuries, it has been the subject of studies of a more or less scientific nature, according to the standards of research of different generations.

Only a few hundred years have passed since medicine and the whole range of human knowledge were one and indivisible. Today, in the light of the tremendous development in all fields, it is only natural that the science of medicine has been broken down into numerous component parts. Progress has been very rapid, particularly during the past few decades, and now more than ever before, we understand the importance of specialization. Admittedly, there is still resistance to the idea, even in the great land of opportunity, your own United States. Harvey Cushing, as we all know, had great difficulty in gaining recognition for his specialty. He, himself, tells the story in words that undoubtedly will become classical: "We all appear to be in the position of taking things away from one another—his problems, be he a practitioner. This has been so from the beginning of Medicine."

The cardiologists of the United States have played a great part, not least through the American Heart Association, in giving cardiology its rank as a specialty. The shape of modern cardiology has been molded by what we may call basic investigators, such as Harvey, Laennec, Einthoven, and innumerable other prominent physiologists, whose original purpose was not necessarily to contribute to the understanding of diseases of the heart. It was not until long after their observations that clinicians in different countries applied these basic scientific discoveries to cardiological problems. An army of indefatigable specialized workers have, each in his own way, helped to build up modern cardiology, of which clinical electrocardiography, cardiovascular roentgenology, and pathophysiological hemodynamics are the main supports. But we are still only at the beginning. Think, for example, of how Einthoven's great contribution has developed! In 1903 he published his most remarkable paper on electrocardiography, but it took more than a generation of painstaking research by cardiologists to evolve the empirical method whereby the physiological and the pathological in records of the electric potentials of the cardiac activity can be distinguished. A great many workers in different parts of this continent have produced a tremendous variety of results with the chest-lead technique, which admittedly are indispensable, but the significance of which we have not yet grasped. Frank Wilson's work is classic.

Roentgen's discovery was of enormous importance in giving us an objective view of the configuration and function of the heart, and its most recent result is the method of examining the heart and the vascular system with the help of contrast medium. Thanks to Laubry, Castellanos, Robb and Weiss, Chávez, and Dorbecker, among others, this diagnostic method has come to have decisive importance, particularly in the congenital heart anomalies.

In the field of hemodynamics, the basic research was done by Ludwig, Otto Frank, Krogh, Starling, Wiggers, Katz, Bernstein, Liljestrand, and U. von Euler,

who stimulated later clinical studies on circulation. From being limited to fairly simple bedside observations that were clinical in the strict sense of the term, clinical cardiological research has been transported into the laboratory, where it has been enriched by basic research in widely varied fields. Who would have dreamed, for instance, that atomic energy would come to have significance for the study of circulation? The radioactive isotopes have become the new microscope in medicine.

It might seem that the problems concerned are of theoretical interest only; but this is far from the case. Scientific discoveries must be the foundation upon which we base our actions, but at the same time the physician, and particularly the heart specialist, must understand and help the patient as a human being. We have all seen how diseases of the heart, blood vessels, and circulation have increased under the stress of modern life to the point where they are becoming a grave problem not only for the individual, but for society as a whole.

A Congress such as this provides an opportunity for personal exchange of laboratory findings and clinical experiences, which, in addition to adding to our knowledge, stimulates us to fresh endeavor.

As a European, I regret that we do not have with us today our Nestor, that great teacher, Laubry of Paris, nor that distinguished physician, Sir John Parkinson of London. It is gratifying, however, to note that many of the men who belong to the future in Europe have been able to join us. We have come together to exchange thoughts, to learn, and to observe, and the program gives promise that our high expectations will be more than fulfilled. I am convinced that all of our European friends, both those who are here today and those who were unable to come, will join me in extending heartfelt thanks to the hospitable United States and particularly to Dr. Louis Katz and his colleagues in the Third Inter-American Cardiological Congress.

PRESIDENTIAL ADDRESS BY DR. LOUIS N. KATZ

DISTINGUISHED guests, official delegates, members of the Congress, ladies and gentlemen: May I first of all express my own personal appreciation and that of my institution, the Michael Reese Hospital, for the confidence you placed in us in accepting Michael Reese Hospital as host of this Congress and in authorizing me to be its President. We consider this a special honor because this Congress is the first Inter-American Cardiological Congress to be held in the United States. We hope that you have been satisfied with the conduct of the Congress and I am sure that you will forgive us if it has failed to come up to your expectations in certain respects. The standards set at the First and Second Inter-American Cardiological Congresses in Mexico City by the Instituto Nacional de Cardiologiá de México, under the able leadership of its Director, Dr. Ignacio Chávez, were so high, you will admit, that it would be difficult, indeed, to approach them. We did our best.

I wish to take this occasion to thank for their untiring effort the many organizations and individuals who assisted me in this Congress. In particular, I wish to thank the local Committee, and especially the Chairman and Secretaries of the several Sub-Committees for their able and diligent participation. Above all, special appreciation must be given to the two persons to whom the major credit for the organization and arrangements of this Congress must go, namely, Mrs. Marie Cole de Pardo, Executive Secretary of the Congress, and my associate, Dr. Richard Langendorf, its Secretary-Treasurer. Both have worked hard and intelligently—yes, even "beyond the call of duty." A word of thanks should go also to the many volunteers who have given of their time. And finally, may I thank all of you for your patience and tolerance.

I cannot resist the temptation on this occasion to talk to you briefly about the future in the field of cardiovascular diseases as I see it. We have here with

us today some of the finest research talent from the Western Hemisphere, from Europe, and even from the far corners of the world, gathered to discuss work we have accomplished, to exchange ideas, to stimulate one another so that we may go back to our clinics, our hospitals, our medical schools, and our laboratories to continue the good work done in the past. This is truly an international gathering without the turmoil and discord that is found in international political meetings because we are all working through our discipline, cardiovascular science and medicine, for a common goal, the benefit of man. As is true of most scientific gatherings, we are imbued with the merits of our worthy cause and have little time for the squabbles that plague other international gatherings. This is good.

It is remarkable also that we have in our midst eminent internists, surgeons, roentgenologists, pathologists, physiologists, pharmacologists, biochemists, biophysicists, bacteriologists, and other specialists. I think this represents a new fruitful departure from the traditional separation of these disciplines in the past. Here, we men and women of varying scientific and medical backgrounds are gathered together to think through the problems of diseases affecting one of the major organ systems of the body: diseases which in a country like the United States are the leading causes of disability and death, far above all others. As we review what has been accomplished in the last quarter of a century, what has happened in the two years since the Second Inter-American Cardiological Congress, and what is being presented at this Congress, we have great cause for pride in our accomplishments.

It is interesting that the traditions of Europe remain, that European influence has spread to the Middle East, to the Far East, to Oceana, and to both North and Latin America. We can see how there has grown up in the Western Hemisphere a magnificent discipline with many minds and many institutions devoted to cardiovascular diseases. But to me, it is far more significant to have watched the recent tremendous growth of the discipline of the study of the circulation in Latin America; the amazing institute headed by Dr. Alberto Taquini in Buenos Aires and the finest of all institutes in our field, located in Mexico City, the National Cardiological Institute of Mexico, with its affiliated departments of fundamental medical sciences, with its magnificent complement of distinguished physicians and investigators, all integrated by my good friend, that able leader, the founder of the Inter-American Society of Cardiology and its Permanent Honorary President, Dr. Ignacio Chávez. This institution in Mexico City and its personnel have not been excelled in the past. Through this institution, Mexico has set a standard which should be striven for in other parts of the world.

It seems to me that the approach of this Mexican institution is the one required to attack and conquer the diseases of the heart and blood vessels more effectively and more rapidly than has hitherto been possible. What is more exciting and productive than the gathering together of experts of various backgrounds dedicated to the diagnosis, care, and prevention of this important group of diseases? The constant interplay of a coordinated team is bound to lead to important positive discoveries, as those of us who were in Mexico had the good fortune to witness. I was personally delighted that we had the opportunity Tuesday night to see a film of this institution presented by Dr. Chávez. I insist that the future of cardiology, in its broadest terms, is dependent upon the creation of many such institutions throughout the world. This, together with the meeting from time to time of physicians and scientists of all countries interested in cardiology, is the hope of the future.

It is obvious, however, that it is not enough to have magnificent institutes and splendid staffs; we must define our objectives more precisely. What is it that we are aiming for? It is obvious that we are trying to improve our diagnostic skills so that we may be better able to recognize diseases of the circulation

earlier and to define the varieties more precisely. It is obvious that we must know the geographic distribution of these diseases and their natural history so that we may, throughout the world, be better prepared to recognize and cope with them, and be better equipped to prognosticate the future of patients afflicted with these diseases. But these are not ends in themselves; we must strive to improve the treatment of the diseases of the heart and blood vessels, to counteract heart failure and circulatory failure, to make it less empiric and more scientific, and to establish precisely what can be hoped for from surgery of the heart and blood vessels. While we must not discount authority and the accumulated knowledge of the past, we must not, on the other hand, revert to the stagnant era of uncritical dogmatism and scholasticism which followed Galen for a long time.

The progress in diagnosis, prognosis, and management has been gratifying, indeed. It would be pointless for me to attempt to narrate the important discoveries which have been made. You are all as keenly aware of them as I am. However, it might be worth while to pause a moment and compare the attitude to diseases of the circulation now and thirty years ago, when I first became interested in the subject. I can recall vividly how unsatisfactory our knowledge was at that time. Diseases of the heart and blood vessels were considered necessary evils which were inflicted upon mankind and which had to be tolerated. The highest aim in the field of cardiovascular diseases seemed to be to see how precisely during life one could make the necropsy diagnosis. It was a period of therapeutic nihilism. There was little effort, so it seemed to me, to reverse the process. Today things are different. Many forms of heart disease can be arrested, some can be reversed, and some are even cured. There is no question but that the result of our work is the substitution of the new psychology of hope for the old psychology of fear.

As a by-product of this positive approach, one important development has occurred within the last decade, namely, cooperative study involving many people and many institutions. For example, this was the case in the evaluation of quinidine derivatives under the leadership of Dr. Paul D. White. This has been the case in the investigation, under the leadership of Dr. Irving Wright, of the value of dicumarol in recent myocardial infarction. I can see great promise of real accomplishment by such cooperative studies in the future, in which the individual physician and investigator and the individual institution is able to merge the competitive spirit in an integrated cooperative study, because it is recognized that the information and benefits to be derived are far greater than could be achieved by each one working independently.

The aim of medicine is broader than the endeavor to diagnose, prognosticate, and manage disease. Far more important, as we all know, is prevention. There is a vast area of study still remaining in preventing cardiovascular disease, despite the considerable knowledge that has accumulated on this subject. More and more of our efforts, I believe, should be directed toward this goal.

Finally, we should stop and pause and ask ourselves: What are the major basic problems in our field? I am sure that you will unanimously agree that based on their importance, there are three fundamental problems at the present time, the solution of which will be epoch making.

First, what is rheumatic fever? What is the organism which is responsible for it? Is it a virus? Is allergy involved? What is the role of the collagenous tissue? Is rheumatic fever a response by the host of a set kind to a single outside agent, or are a multiple of agents involved, all leading to a similar response?

Second, why high blood pressure? Despite the brilliant work of the Buenos Aires school of Drs. Braun-Menéndez, Taquini, Fasciolo, and others, under the able leadership of Dr. Houssay, despite the fundamental work of Dr. Goldblatt,

the question still remains: What precisely is the role of the kidney in the pathogenesis of this disease? Is hypertension neurogenic, psychosomatic, or is it due to some hitherto unresolved hormonal disturbance? What is the nature of the primary involvement of the blood vessels? What makes hypertension become fixed? What is the role of habitat and environment and diet?

Third, what is the cause of hardening of the arteries? Surely, it is not simply aging. Aging is an expression we use too often to hide our ignorance behind. What is the role of the nourishment of the blood vessel wall in its genesis? What is the part played by the lipids and cholesterol? How far does diet aid in its development? Is it a long-term effect of some neurogenic or hormonal disturbance?

Rheumatic fever and rheumatic heart disease, essential hypertension, and atherosclerosis are the principal causes of heart disease. Real progress in the eradication, in the alleviation, in the management, and in the prevention of these diseases must await answers to the pathogenesis of these major disabilities. These are difficult problems to solve. They demand the full-time cooperative energy of the ablest among us, clinician and investigator alike. They demand the full-time activity of our best intelligence. We need the services of many teams consisting both of mature and of promising young men to concentrate on these problems, men who will devote their lives to a concerted attack, men who will not be discouraged if for years they have little or nothing to report. Men willing to dedicate their lives to the study of these major problems should be assured an adequate income, should have adequate facilities for their research, should be provided with sufficient technicians and experts in allied fields so that they may follow their ideas unrestrained wheresoever they may lead them. This is the lack at present as I see it. This is the need that must be met in the future. Should this need be met in generous fashion, I am sure that the answers to the major problems will be forthcoming, perhaps sooner than we imagine, perhaps even in the life-time of the younger ones among us. Then we shall be repaid manifold for our efforts and we shall have realized to the full the promise held forth in this Congress which we have created.

Thank you.

THANATOPHAGIA, DANGERS OF DINING

DR. HOWARD B. SPRAGUE

AN ADDRESS MADE AT THE BANQUET OF THE CONGRESS

I APPRECIATE the honor of being invited to address you even though I realize that I am only a substitute in place of your original entertainer. The appreciation of such an honor by an after-dinner speaker, however, is always diluted by the realization that he is not expected to say anything of importance. That, however, is proper, since at a medical conference of cardiologists the evening banquet should be the diastolic, or resting, phase of the meeting.

I also apologize to our Latin-American members for speaking to you in my native language. I am reminded of an incident of the war in which a naval officer told of meeting in the wardroom of a foreign allied vessel a group of officers representing seven nations. "Fortunately," he said, "we were all very fine linguists, that is, we all spoke English."

When Dr. Katz got in touch with me a week or so ago to ask me to give this talk, he used an agent more terrible than the atom bomb, that is, the long-distance telephone, which permits the victim no time for thought or excuses, and I found it easier to say "yes." He told me that I could talk on any subject, and so I have made up a subject for you. I contrived the word, Thanatophagia, from the Greek Thanatos, meaning "death," and phagia, "eating." Thus, we have death-eating, or the Dangers of Dining. It should remind us all of the

Ninth Century Arabian proverb that "the two greatest hazards of an aging man are a good cook and a young wife."

I shall not discuss all the dangers of dining. I well remember the days when Richard Cabot used to caution us, as students, that at the onset of any disease, the patient, or some member of his family, could always remember something that he had eaten that must have been responsible. There are, of course, the dangers of gorging and of the "acute indigestion" of the pre-Herrick days. On one occasion I had the opportunity of saving the life of a friend of mine who, after a bevy of Martinis, tried to swallow too large a piece of steak.

But concerning that of which I now speak, and here demonstrate as an apparently harmless white powder in this bottle, I feel like one of the Borgias. This is a substance which is contained in the bodies of all of us here; one-half of it is in our brains. Each of us possesses within him about 50 grams, which is worth, at retail, about $3.75. But for the past thirty-five years it has steadily gained in prominence as the villain in our daily lives. I refer, of course, to cholesterol. That not all of you are terrified of it is shown by your consumption of this meal, which has probably provided you with the average daily intake of one-third of a gram. Like women, it is something difficult to live with or without.

I feel that I am invading the field of my friends, Louis Katz and George Herrmann, in discussing cholesterol and coronary disease, but I believe it is legal for me to do so since even we at the Massachusetts General Hospital are working on the subject, though with a rather different approach. We are trying to find out what kinds of people acquire the disease, rather than what kinds of animals can be made to develop it.

The first unhappy beast to succumb to atherosclerosis by heavy, prolonged dosage with cholesterol was the rabbit, and he can quite readily be made to develop it. On the other hand, carnivorous animals do not develop it naturally; Fox, from his fascinating work at the Philadelphia Zoo, states that no wild rodent ever gets atherosclerosis. Omnivorous animals, if sufficiently debauched by investigators, will acquire it. Katz and Herrmann can accelerate it in chickens with high-cholesterol diets, but chickens normally develop it with age. Steiner and his associates have finally produced it in dogs by a combination of cholesterol feeding and a disturbance of thyroid function with thiouracil.

As for man, atherosclerosis, as Dock points out, is rarely seen in people with diets high in whole cereals, beans, and vegetable oils, whereas it is common only in those with diets rich in animal fats but poor in animal viscera, and especially in diets with much milk, fat, and egg yolk.

Arteriosclerosis, implying largely a medial affair, a picture of fibrosis, desiccation, and calcification, comes normally in chickens, eagles, elderly cows, and gourmandizing, irregularly eating carnivora; but Fox has shown that old, male parrots have atheromatous possibilities in their vessels beyond those of any mammal except man. The parrot is probably also the only other creature which would be invited to give an after-dinner speech.

Commander P. E. Steiner of our Naval Reserve Medical Corps contributed very suggestive data to our knowledge of this subject in his autopsy studies during the war of undernourished native Okinawans. He found that they did not suffer from coronary disease, but demonstrated that they had long, capacious, tortuous, large intestines like herbivorous animals. They eat predominantly a vegetable diet of sweet potatoes and rice; a diet low in fat and protein and with the protein mainly from soybean. They have little meat and milk. From this demonstration we might take a more positive stand about such a diet than did Dr. Hutchinson when he said that, in general, a vegetarian diet was harmless, but tended "to fill a man with wind and self-righteousness."

Our own Dr. Chávez has shown, for example, that hypertension, angina pectoris, and coronary thrombosis were uncommon in Mexican Indians in spite of

the fact that arteriosclerosis was as common as in white subjects. Kuczinski found that Kirgiz nomads with high-fat diets had a marked incidence of atherosclerosis, while their contemporaries in the towns, living on a mixed diet, did not.

It is of interest that Eskimos on high-meat diets have low blood pressures, relatively low blood cholesterols, and high basal metabolic rates. Those of you who have seen Commander MacMillan's motion pictures will recall their eating habits, especially their netting, skinning, and consuming raw the entire bodies of small auks which they dip out of the air.

The whole subject of blood cholesterol is very confusing, however. Pyknic individuals are said to have higher cholesterol levels than asthenic individuals, which complicates the situation in relation to normal standards since our work so far seems to confirm the tendency to mesomorphy in premature coronary disease in men. Katz has recently noted that his chickens on a low-fat diet had a higher blood cholesterol than those on a high-fat diet. This raises the questions involved in the reaction to starvation and all the complexities of endogenous cholesterol.

I wish to touch on one other paradox, that of the teeth. Wild animals usually die because they lose their teeth, and suffering from malnutrition, become easy victims of the elements or their enemies. This is negative thanatophagia. Men, on the other hand, seem to live longest on diets which are bad for their teeth. New Zealanders, with the longest life expectancy of all, have much dental trouble.

This reminds us of McCay's famous rats. He found that diets satisfactory in food elements, but so low in calories as greatly to retard maturity in the rat, resulted in pronounced lengthening of life. Well-fed, handsome young rats succumbed earlier in life. It makes one wonder about our own pediatric concepts.

Perhaps we can, for a moment, defend the egg. For the sake of our Latin-American friends here tonight we may remind ourselves that Columbus first made the egg stand up for itself, and, from a practical point of view, in the ordinary man, cholesterol, as such, may be less important than fat. I refer, of course, to the recent presentation of Moreton in relation to the physical state of the plasma lipids. It is his contention that the explosive delivery into the blood stream of large fat particles coincident with repeated heavy fat meals provides the mechanical insult to the coronary intima similar to what occurs in the persistent hyperlipemic states, such as diabetes, which are notorious precursors of atherosclerosis.

What may be some of our inconclusive conclusions at this point? First, the effects of the ingestion of fats and cholesterol are but partial factors in the equation. True, we may be dealing with essentially a quantitative problem in various experimental animals, but this does not apply clinically to man. That is, there are different kinds of men and different reactions to diet. There may well be herbivorously constructed men, like rabbits, and carnivorously constructed men. Perhaps we would find out more about coronary disease by studying the types of large bowel possessed by men than by recording their blood cholesterol levels.

Nor does this explain woman's relative freedom from coronary disease. I dare not say here that such conclusion is well founded, but one might imagine that woman was essentially a predatory carnivorous animal—I did not say "rodent."

It may also be lamentably suggested from racial studies that the price of freedom from coronary disease may be cirrhosis of the liver, since this is common in peoples relatively immune to atherosclerotic tendencies.

I believe, however, that men should live on diets very low in fats and cholesterol if they come from "coronary" families, are predominantly mesomorphic in body type, and especially if they have seriously encroached upon their normal fat deposit areas.

It was of interest to me two years ago to examine, at my own request, the oldest living graduate of Harvard College. He will be 103 years of age next month. He is a healthy, spare individual with normal physical findings except for visual and hearing defects. His electrocardiogram is normal. I hesitate to mention this in the presence of Dr. Wilson, but I recorded CF precordial leads rather than V leads. I recently asked his wife about his dietary habits. This is her reply. "As to Mr. Adams' diet, he has an excellent appetite and can eat anything except pork. He eats any strip of fat on meat. He never salts his food at the table as it is well seasoned in the kitchen. He has top milk on cereal, not heavy cream. All his life his breakfasts have been cereal, boiled egg, and coffee, but no bread. In his younger days when he was teaching he ate two boiled eggs every morning. His favorite dessert is apple pie, which he does not have very often, and ice cream, which he has once a week. He is fond of sweets and every day has soft chocolate candies after dinner. He does not care for supper, but always takes a glass of sherry or muscatel with cookies just before retiring."

You will note that this man has eaten eggs every day for one hundred years. I have estimated that he has consumed about 56,000 eggs without acquiring lethal cholesterosis. This is very reassuring to us egg eaters.

In deferring the fatal influence of cholesterol and other factors in thanatophagia, I am reminded of what Marcel Proust once said, "Nature hardly seems capable of giving us any but quite short illnesses, but Medicine has annexed to itself the art of prolonging them."

With this in mind, I decided that I would close with a medical interpretation of a famous quatrain of Omar which may perhaps be used as a prescription for longevity.

"A book of verses underneath a bough"

This refers to the relaxations of the literary life. The "bough" might be, in the winter, in one of our delightful Latin-American countries. In the summer, so far as I am concerned, it could be in Maine.

"A jug of wine, a loaf of bread"

You will note that the jug of wine comes first. I am sorry that Dr. Stroud is not here to comment on this. The loaf of bread is low in cholesterol, can be low in sodium, but should have added vitamins.

"And thou beside me, singing in the wilderness."

The "thou" in this case should be an affectionate, but not too demanding wife, preferably your own. The soothing influence of song is obvious.

"And thou beside me, singing in the wilderness,
Ah, Wilderness were paradise enow."

ANNOUNCEMENTS

DR. ANTONIO BATTRO

At the beginning of the Plenary Session, the President made the following simple statement:

"Dr. Antonio Battro, Professor of Clinical Medicine at the University of Buenos Aires, one of our active members, died unexpectedly of a coronary attack. We shall rise for one minute of silence in his memory."

THE FIRST INTERNATIONAL CARDIOLOGICAL CONGRESS

In the name of the International Council of Cardiology, Dr. Paul D. White made this announcement:

"It has been agreed by the International Council of Cardiology to hold the First International Cardiological Congress in July, 1950, in Paris under the Chairmanship of Professor Charles Laubry, who has appointed a local committee to help him and who will receive advice from the other members of the International Council of Cardiology."

Original Communications

ON THE POSSIBILITY OF CONSTRUCTING AN EINTHOVEN TRIANGLE FOR A GIVEN SUBJECT

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INTRODUCTION

FOR more than a third of a century students of electrocardiography have struggled with the concepts that underlie the equilateral triangle of Einthoven, Fahr, and De Waart, and have continuously debated the validity of the assumptions it involves. During this long period numerous investigators have attempted to settle these disputes by generating an electric field of the appropriate kind in a human cadaver, or in some sort of model, and comparing the experimental results with the theoretical predictions. The more important of these studies have been reviewed in a recent article from this laboratory,[1] and the results of a cadaver experiment, of the kind in question, performed here a number of years ago have now been published[2] in connection with a discussion of the possibility of converting the Einthoven triangle into an equilateral tetrahedron.

It is our present purpose to present and discuss the results of some experiments of this same general sort in which the cadaver, or model, has been replaced by the body of a normal human subject. This substitution offers some very obvious advantages and it involves no very great flight of the imagination. We have wondered why we did not attempt it long ago and from what source came the suggestion that led us finally to make it. The train of thought concerned cannot now be traced to its origin with any certainty, but it may well have been the result of a discussion, in the autumn of 1944, when one of us appealed to Dr. Kenneth S. Cole and Dr. Alvin M. Weinberg for advice as to the best way of measuring the magnitude of the potential variations of a central terminal connected to the limb electrodes through equal resistances. Dr. Cole expressed, on this occasion, some dissatisfaction with the means previously employed for this purpose and intimated that a more direct approach to the problem was preferable and ought to be feasible. Apparently, his first reaction was that it might be

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possible to obtain the desired information by mapping the isopotential lines of the cardiac field on the surface of the trunk. After further consideration, however, he remarked that the problem "might be reversed" by introducing a three-phase alternating current into the body by way of the limb electrodes and finding on the anterior and posterior surfaces of the chest the points at the same potential as the node formed by the three phases in Y or star connection. Some months later, preparations for carrying out this experiment were made but they were never completed, partly because it was found that when two limb electrodes were connected to a source of low frequency alternating current and also to a central terminal, through equal resistances, the location of the line on the body surface corresponding in potential to this terminal was determined chiefly by the relative magnitude of the two "contact" or "skin" resistances involved. The question then arose as to whether the measurement and equalization of these resistances (by the method of equalizing the resistances in the limb leads described by Einthoven, Bergansius, and Bijtel[3]) would not defeat the main purpose of the investigation. Dr. Cole suggested later that we connect the current source to two of the limb electrodes, using each of the three pairs in turn, and plot the points at the same potential as the third. The results of a few experiments of this kind are described in a later section of this paper.

The experiments with which we are at present mainly concerned were begun in September, 1946. We have frequently interrupted them for the purpose of analyzing the results of those already done and of studying the theoretical questions and the technical problems encountered. To a very large extent they have been of an unsystematic, preliminary, and exploratory kind. We are far from satisfied with the data collected thus far and are in the process of trying to perfect the technical procedures required to the point where the variation of the results on repetition of a given experiment will be negligible for our purpose. For this reason, the conclusions suggested by the observations available at this time must be regarded as subject to future revision.

When we began our investigations we were not aware of the work of Burger and Van Milaan[4] of Utrecht, who for several years have been studying electric fields generated in a model of the human body which they have built. Since we have become familiar with their publications we have been considerably influenced by their ideas, and particularly by their elegant method of constructing a triangle which summarizes all the information, concerning the nature of the electrical field in their model, obtainable by measuring the potential differences between electrodes corresponding in location to the limb electrodes used in clinical electrocardiography.

In our earliest experiments, one set of three electrodes was placed on the extremities in the usual way. Three electrodes were also placed on the anterior surface of the body, one just above the symphysis pubis and the other two near the junctions of the arms with the trunk. Three additional electrodes were put on the back and these were located as nearly as possible directly behind the corresponding electrodes of the anterior set. From these nine electrodes the following leads were taken: (1) the usual limb leads (I, II, and III); (2) corresponding leads from the anterior electrodes (IA, IIA, and IIIA); (3) the same

leads from the posterior electrodes (IP, IIP, and IIIP); and (4) a lead from each of the anterior electrodes to the corresponding posterior electrode (RR, LL, and FF).

It should be pointed out that whereas the exact locations of the limb electrodes are a matter of no importance, the positions of the electrodes on the trunk must be determined with considerable precision if consistent results are to be obtained in experiments on different subjects. With this in mind the following plan for placing these electrodes was adopted. Each of the upper anterior electrodes was put in the area bounded laterally by the palpable coracoid process of the scapula and above by the inferior margin of the clavicle. The corresponding posterior electrode was then placed directly behind it and immediately below the scapular spine. The inferior posterior electrode was put in the midline on the lower part of the coccyx, and the corresponding anterior electrode straight in front of it, on the midline and just above the pubic symphysis. Even though considerable care was used in the placement of these electrodes, it seems not unlikely, when we consider that human chests vary greatly in size and shape, that the personal equation involved in deciding upon their exact positions sometimes had an effect upon the relative magnitudes of the deflections in the leads requiring their use.

The electrocardiograms of normal subjects which have been taken by this system of nine leads are all much like that reproduced in Fig. 1. It will be noted that the deflections in Leads RR, LL, and FF are strikingly similar in general outline but very different in magnitude. Those of Lead LL are largest, and those of Lead FF smallest. This is true of all of our records of this kind. In taking these sagittal leads the galvanometer connections were made in such a way that relative positivity of the posterior electrode produced an upward deflection in the completed record. The relations between the nine leads from the electrodes on the front and back of the trunk are expressed by the equations that follow. In these equations the symbols *IA*, *IIP*, *RR*, etc., may be regarded as representing the leads for which they stand, considered as vectors which are to be added vectorially according to the parallelogram law, or as representing the deflections in these leads, which are to be added algebraically.

$$(1) \quad IP + RR = IA + LL$$
$$(2) \quad IIP + RR = IIA + FF$$
$$(3) \quad IIIP + LL = IIIA + FF$$
$$(4) \quad IP + IIIP = IIP$$
$$(5) \quad IA + IIIA = IIA$$

In the experiments in which an artificial field was established in the trunk we employed a vacuum-tube beat-frequency oscillator to generate a current alternating 25 times per second. This current was introduced into the chest by way of two small circular electrodes and was maintained constant by means of a sensitive rectifier-type milliammeter. The diameter of the electrodes, the distance between their centers, and the magnitude of the current passed into the body have varied in different experiments. No systematic study of the effects of these variations has been made, but in general, the potential differences between

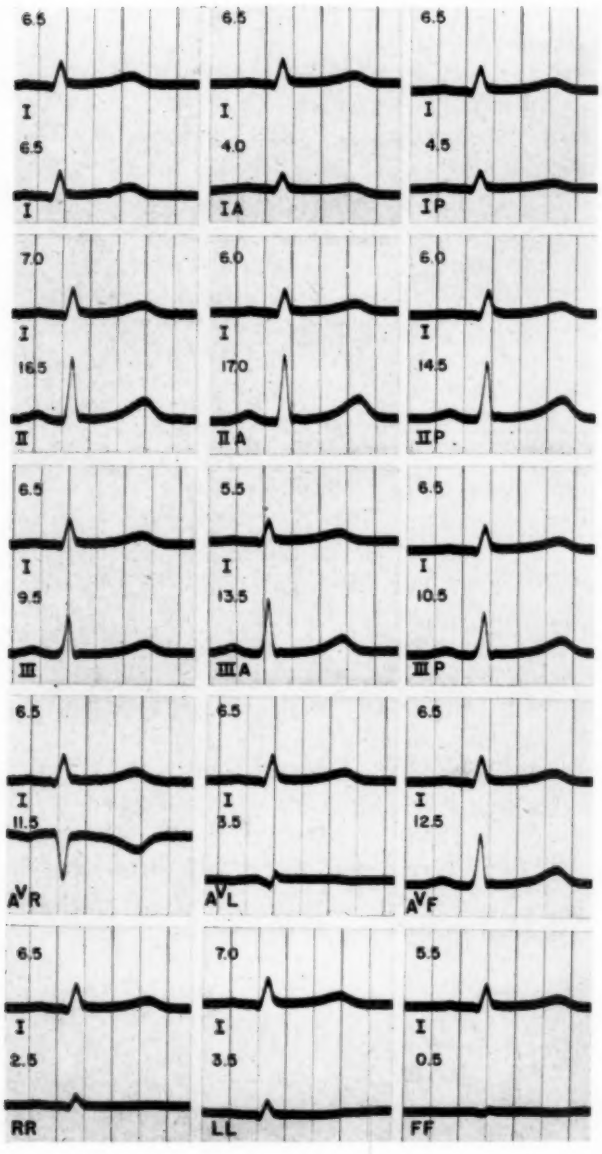


Fig. 1.—Experiment 5, *a*. Electrocardiogram of a normal subject showing the standard limb leads (I, II, and III), the corresponding anterior (IA, IIA, and IIIA), and posterior leads (IP, IIP, and IIIP), the augmented unipolar leads (aV_R, aV_L, and aV_F), and the sagittal leads (RR, LL, and FF).

the extremities have been roughly proportional to the product of the current and the distance between the input electrodes. It will be convenient to refer to this product as the electrical moment.

At the beginning of an experiment a point on the chest was selected and the centers of the input electrodes were placed on a line drawn through this point in such a way as to make the distances of their centers from it equal. In the case of a given subject the electric field established in the trunk by connecting these electrodes to the oscillator is then adequately defined by giving the location of the point mentioned, the distance between the centers of the electrodes, the magnitude and character of the current, and the angle between the line specified and the horizontal. After the first two or three experiments the location and manipulation of the input electrodes was greatly simplified by fastening several pairs of these electrodes to a small circular protractor. This made it possible, after the center of the protractor had been placed over the chosen point, to vary the position of the current axis in the manner desired by selecting the proper pair of connections instead of by removing and replacing the electrodes. We shall speak of the input as vertical when the current axis was parallel to the midsternal line, and as horizontal when this axis was perpendicular to this line.

Since alternating current was employed, the current axis had one direction during one-half of the cycle and exactly the opposite direction during the other half. The deflections recorded by the various leads used are, therefore, sine waves (considerably distorted in some instances). The measurements given represent the full amplitude of these waves minus the width of the light beam, which is about 2.0 millimeters. Plus and minus signs have been assigned to these measurements in such a way as to fulfill Einthoven's law whenever this law could be applied. In some instances each lead was taken simultaneously with Lead I, and when this was done deflections which were in phase with those of Lead I were considered positive and deflections which were 180° out of phase with those of Lead I were considered negative, or vice versa. For reasons which will appear later, the deflections of Leads RR, LL, and FF were made opposite in sign to those of unipolar Leads V_R, V_L, and V_F, respectively, except when the current axis was parallel to the sagittal plane, in which case they were considered all positive or all negative.

AN ILLUSTRATIVE EXPERIMENT

The experiment illustrated in Figs. 2,*A* and 2,*B* and summarized in Table I was performed on Sept. 24, 1946. A current of 0.5 milliampere was passed through the trunk by way of electrodes 1.1 cm. in diameter, which were equidistant from a point 4.0 cm. to the left of the midsternal line and at the level of the fourth intercostal space. The distance between them was 5.0 centimeters. The various leads were taken with the current axis horizontal and repeated after this axis had been rotated clockwise through 30, 60, 90, 120, and finally 150 degrees. The deflections in each of the records were measured and Einthoven's manifest potential difference, E, and the angle made by the electrical axis with the horizontal were computed in the customary way for each set of standard limb

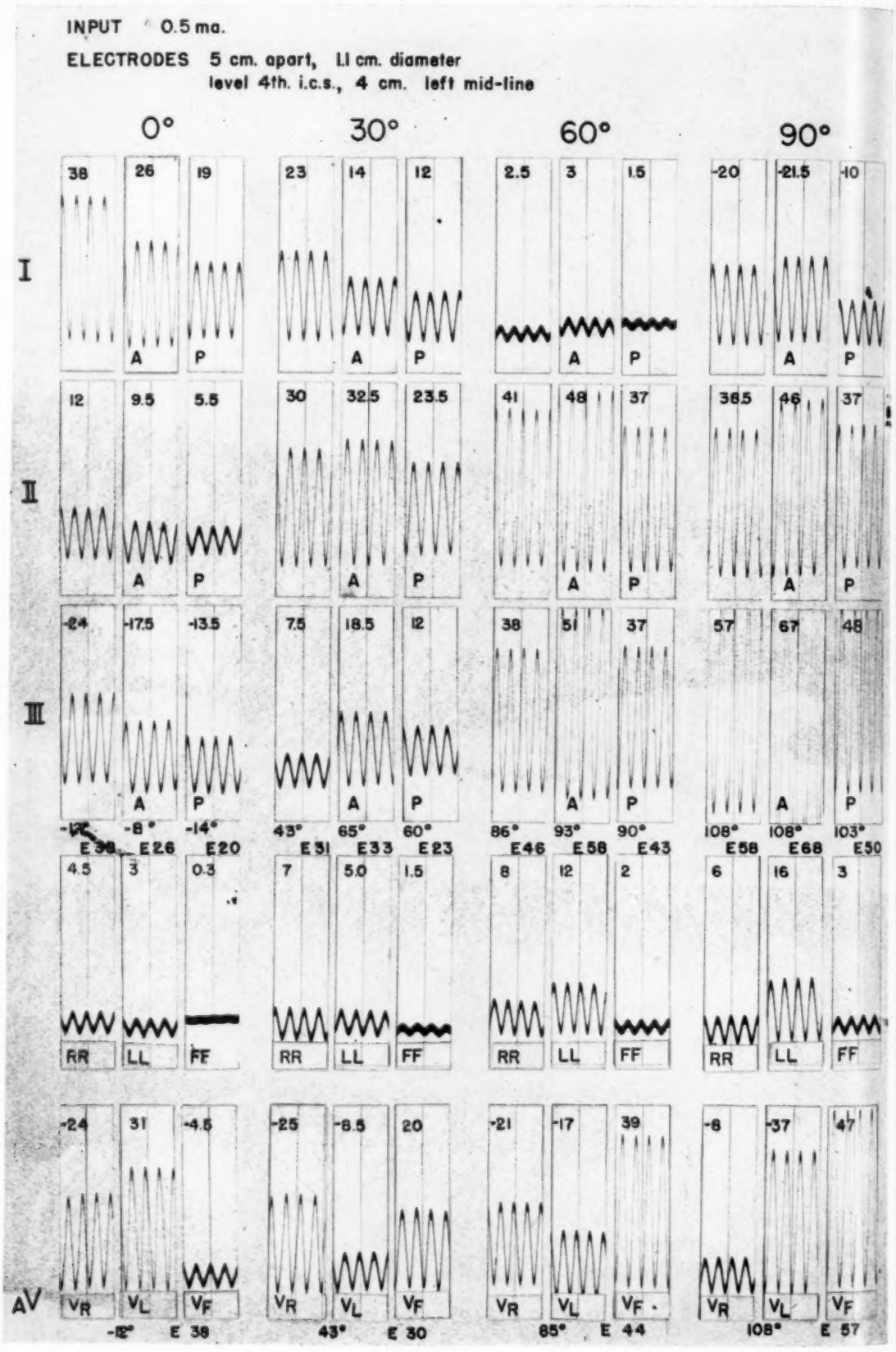


Fig. 2.—*A*, Experiment 3, *b*. Input electrodes to the left of the midline. Deflectons in the various leads when the angle made by the current axis with the horizontal was 0, 30, 60, and 90 degrees, respectively.

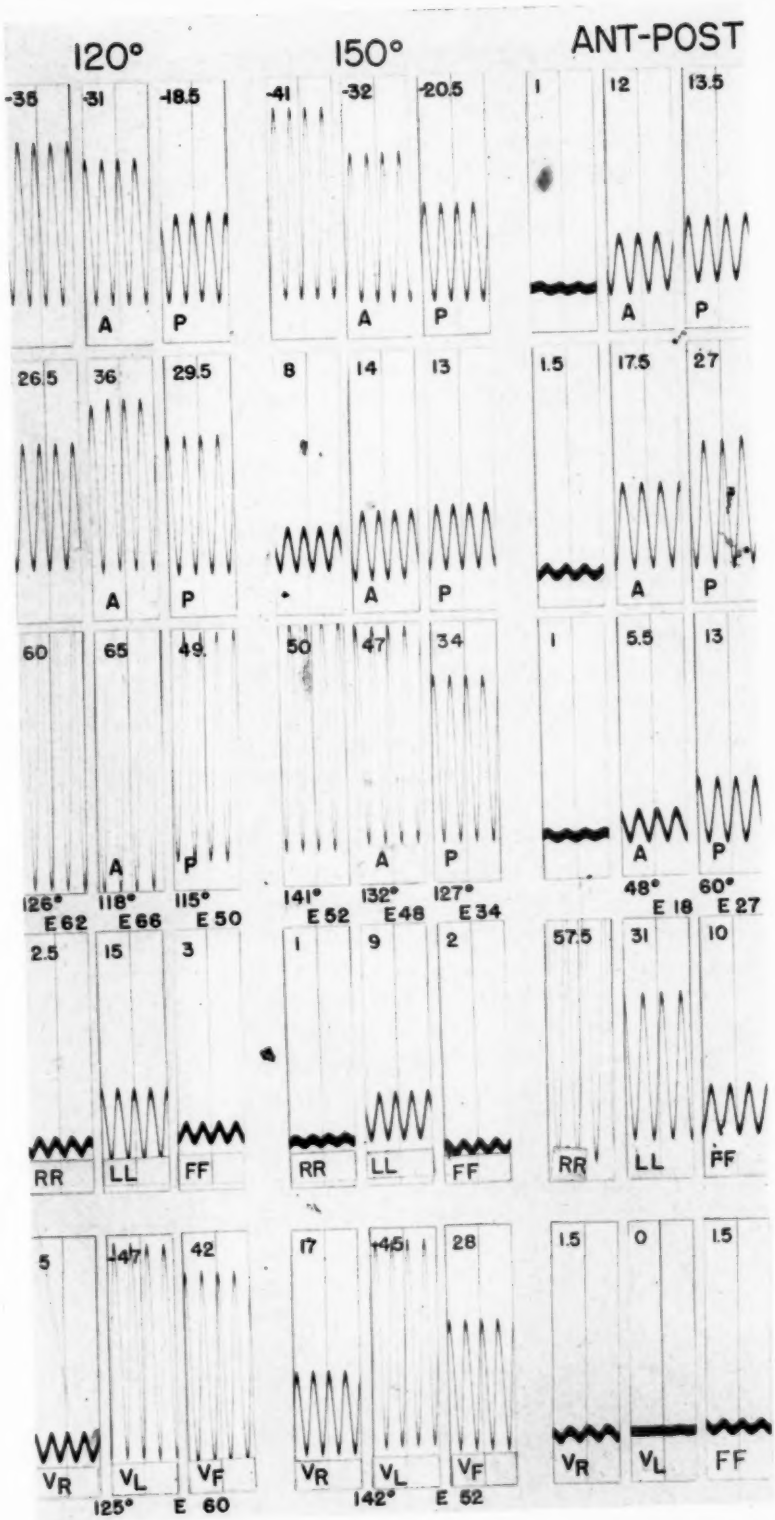


Fig. 2.—*B*, Experiment 3, *b*. Continuation of Fig. 2, *A*. Deflections in the various leads when the angle between the current axis and the horizontal was 120 and 150 degrees, and anteroposterior when one input electrode was on the back and the other on the front of the chest.

leads, unipolar limb leads, anterior leads, and posterior leads. The values for these quantities which appear in Figs. 2,*A* and 2,*B* were obtained graphically. Those which are given in Table I were computed. In the case of those measurements which did not fulfill Einthoven's law, the measurement for Lead III was revised, for the purpose of these computations, to the extent required to bring it into accord with those for Leads I and II.

The last set of leads shown in Fig. 2,*B* was taken at the end of the experiment for the purpose of studying the field produced by a sagittal current axis. One electrode was placed on the front of the chest, at the level of the fourth intercostal space and over the right margin of the sternum, and the other on the back, close to the seventh dorsal spine. The two input electrodes were then far apart and, since the current was not reduced, the electrical moment was much greater than when the other records were taken. It will be noted that the deflections in the standard limb leads are extremely small; in other experiments it was found that they could be abolished altogether by moving one of the input electrodes a short distance in one direction or another. It was never possible, however, to bring the deflections to zero in all of the standard limb leads and in all of the anterior or posterior leads at the same time. When the current axis has a sagittal direction the deflections in the sagittal leads, RR, LL, and FF, are naturally larger than when this axis is parallel to, or makes a small angle with, the frontal plane. In the few experiments of this kind performed, however, the deflections in Lead FF were always smaller, and usually much smaller, than those of Leads RR and LL.

Before discussing other aspects of this experiment we shall explain the figures enclosed in parentheses in Table I. In general, any number of forces acting at the same point can be added vectorially according to the parallelogram law, or can be regarded as equivalent to three forces each parallel to one axis of a system of mutually perpendicular axes equal in number to the dimensions of the space under consideration. It has always been held that the electromotive force of the heart at a given instant is a directed quantity of this kind, and this view is certainly correct if the electrical field of the heart is equivalent to that of a mathematical dipole, as Einthoven and his associates assumed. In the experiment under consideration, the distance between the positive and negative poles was not, as in the case of such a dipole, extremely small in comparison with the distance of the lead electrodes from them. It seemed desirable, therefore, to ascertain whether, for example, a current input of 0.3 milliamperes at 30 degrees was equivalent, under these circumstances, to a current input of 0.3 cos 60° milliamperes at 0 degrees plus a current input of 0.3 sin 60° milliamperes at 90 degrees. The cosine of 60 degrees is 0.5 and the sine 0.866. If we multiply the observed deflection in Lead I listed under 0 degrees in the table by the former, we obtain the figure 19.0. The deflection for the same lead listed under 90 degrees is −20.0, and this multiplied by 0.866 gives −17.32. The expected deflection in Lead I for a current axis of 60 degrees is then the algebraic sum of these two figures, or 1.68. The observed value is 2.5. For a current axis of 30 degrees the deflection in Lead I measured 23.0 millimeters. The calculated amplitude of this deflection is 22.9 millimeters. If the other figures given in the

TABLE I. MAGNITUDE OF DEFLECTIONS, MANIFEST POTENTIAL DIFFERENCE (E), AND THE ANGLE MADE BY THE ELECTRICAL AXIS WITH THE HORIZONTAL AS DETERMINED IN EXPERIMENT 3b.

CURRENT AXIS	0°		90°		30°		60°		120°		150°		AP
LEAD													
I	38.0		−20.0		23.0		2.5		−35.0		−41.0		1.0
					(22.9)		(1.7)		(−36.3)		(42.9)		
II	12.0	−12°	38.5	110°	30.0	42°	41.0	82°	26.5	125°	8.0	141°	1.5
		38.9		59.4	(29.6)	31.1	(39.3)	42.4	(27.3)	63.8	(8.8)	55.3	
III	−24.0		57.0		7.5		38.0		60.0		50.0		1.0
					(6.7)		(37.6)		(63.6)		(51.8)		
IA	26.0		−21.5		14.0		−3.0		−31.0		−32.0		12.0
					(11.8)		(−5.6)		(−31.6)		(−33.2)		
IIA	9.5	−9°	46.0	108°	32.5	68°	48.0	96°	36.0	118°	14.0	132°	17.5
		26.3		69.0	(31.2)	31.5	(44.5)	54.1	(35.1)	67.3	(14.8)	49.1	
IIIA	−17.5		67.0		18.5		51.0		65.0		47.0		5.5
					(19.6)		(50.2)		(66.7)		(48.0)		
IP	19.0		−10.0		12.0		1.5		−18.5		−20.5		13.5
					(11.5)		(0.8)		(−18.2)		(−21.5)		
IIP	5.5	−14°	37.0	102°	23.5	60°	37.0	89°	29.5	112°	13.0	127°	27.0
		19.2		49.5	(23.3)	23.4	(34.8)	39.2	(29.3)	48.2	(13.7)	35.4	
IIIP	−13.5		48.0		12.0		37.0		49.5		34.0		13.0
					(11.8)		(34.0)		(47.4)		(35.2)		
AV_R	−24.0		−8.0		−25.0		−21.0		5.0		17.0		1.5
AV_L	31.0		−37.0		8.5		−17.0		−47.0		−45.0		0
AV_F	−4.5		47.0		20.0		40.0		42.0		28.0		1.5
RR	4.5		6.0		7.0		8.0		−2.5		−1.0		57.5
					(6.9)		(7.5)		(−2.9)		(0.9)		
LL	−3.0		16.0		−5.0		12.0		15.0		9.0		31.0
					(−5.4)		(12.3)		(15.3)		(10.6)		
FF	0.3		−3.0		−1.5		−2.0		−3.0		−2.0		10.0
$(V_T)_P-(V_T)_A$	0.6		6.3		0.2		6.0		4.8		2.0		

The theoretical magnitudes of the deflections are shown in parentheses directly below the observed magnitudes.

For each set of standard limb leads, anterior leads, and posterior leads, the manifest potential difference E and the angle which gives the position of the electrical axis, found by the customary method, are given following the figure for the deflection in Lead II, Lead IIA, and Lead IIP.

table are examined it will be seen that, considering all the possibilities of error involved, the agreement between the observed and calculated deflections is surprisingly good. Hereafter, when the distance between the input electrodes was not greater than 5 cm., we shall confine the discussion chiefly to the tracings obtained when the current axis was horizontal and those obtained when it was vertical. It will be convenient to use the letter H to designate the former and the letter V to designate the latter. Such symbols as $(I)_H$, $(II)_H$, $(II)_V$, and $(III)_V$ will be used to represent the deflections in the various leads under these two different conditions.

The sagittal leads RR, LL, and FF measure the differences in potential between the apices of the triangle formed by the posterior leads and the corresponding apices of the triangle formed by the anterior leads. These relations are expressed by the following equations:

$$(6)\quad (V_R)_P - (V_R)_A = RR$$
$$(7)\quad (V_L)_P - (V_L)_A = LL$$
$$(8)\quad (V_F)_P - (V_F)_A = FF$$

Here the symbol $(V_R)_P$ represents the true potential of the electrode on the posterior aspect of the right shoulder and the other symbols have a like significance. If these equations are added and the sum is divided by three, we obtain the expression

$$(9)\quad 1/3\,[(V_R)_P + (V_L)_P + (V_F)_P)] - 1/3\,[(V_R)_A + (V_L)_A + (V_F)_A] = 1/3\,(RR + LL + FF)$$

or, what amounts to the same thing,

$$(10)\quad (V_T)_P - (V_T)_A = 1/3\,(RR + LL + FF)$$

where $(V_T)_P$ is the potential of a central terminal connected through equal resistances to the three posterior electrodes, and $(V_T)_A$, the potential of central terminal connected through equal resistances to the three anterior electrodes. When the sum in the second member of this equation is positive, the anterior terminal is negative with respect to the posterior.

In Table I the figure obtained by adding the deflections in Leads RR, LL, and FF algebraically and dividing the sum by 3 is given for each position of the current axis. Observe that the calculated difference in potential between the two central terminals was small when the current axis was horizontal or nearly so, and relatively large when this axis was vertical or nearly vertical. The anterior terminal is negative with respect to the posterior for all of the positions of the current axis listed.

There is a rough correspondence between the relative size of the deflections in the unipolar leads from the two arms and the relative size of the deflections in Leads RR and LL. In the three instances in which the deflections in Lead aV_L are very much larger than the deflections in Lead aV_R, the deflections in Lead LL are much larger than those in Lead RR (Table I, columns headed 90, 120, and 150). In one instance (Column 30) the deflections in Lead aV_R are much larger than those of Lead aV_L and the deflections of Lead RR are somewhat larger than those of Lead LL. In the other two cases this relation does not hold;

in one of them (Column 0) the deflections of Lead aV_L are considerably larger than those of Lead aV_R, but the deflections of Lead LL are smaller than those of Lead RR; in the other (Column 60) the opposite is true. The deflections in Lead FF are very small for every position of the current axis and it is difficult to demonstrate any relation of the kind in question between this lead and Lead aV_F.

Compared to the apices of the anterior triangle, the corresponding apices of the posterior triangle are more distant from the input electrodes but otherwise similarly situated with respect to them. One would, therefore, expect that when the potential of a given apex of the former became positive or negative the potential of the corresponding apex of the latter must show a fluctuation of the same sign but of smaller magnitude. The coccygeal and pubic electrodes are farther apart than the two electrodes of the other two pairs, but they are also much farther from the precordium. Does this account for the smallness of the deflections in Lead FF? Are the potential variations of the leg electrode regularly smaller than those of the arm electrodes even when the current axis is vertical? These questions cannot be answered now, but we are confident that they can be answered in the near future.

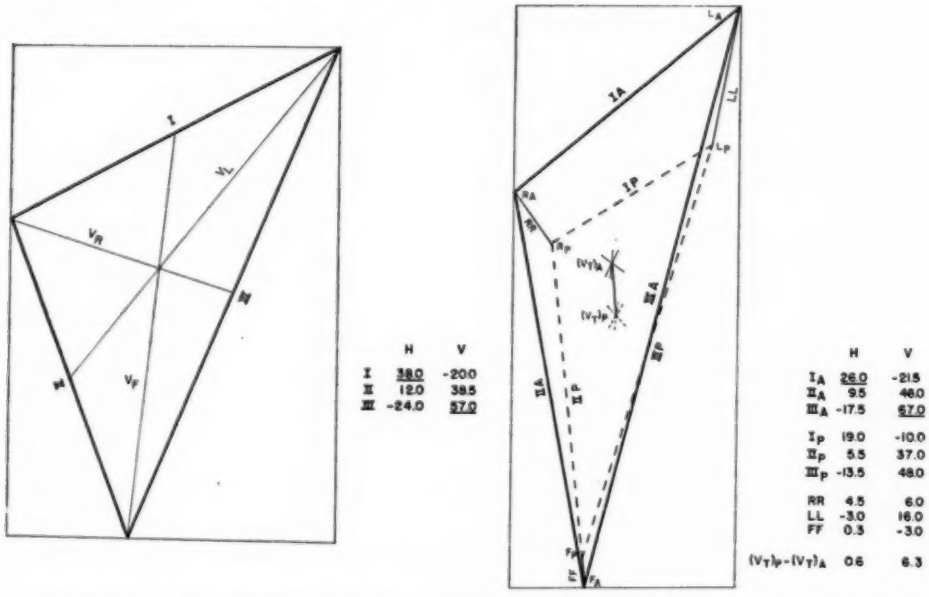
CONSTRUCTION AND USE OF THE BURGER TRIANGLE

Referring once more to the data shown in Table I, we may point out that the magnitude of Einthoven's manifest electromotive force (E) shows striking variations with the position of the current axis. It is much larger for a vertical than for a horizontal axis and is greatest when the current flow is parallel to Lead III (120 degrees). There are also pronounced discrepancies between the position of the axis defined by the input electrodes and the position of the electrical axis calculated in the customary manner. When the former axis made an angle of 60 degrees with the horizontal, the latter was separated from it by an angle of 22 degrees when the calculations were based on the standard limb leads; 36 degrees when they were based on the anterior leads; and 29 degrees when they were based on the posterior leads. For this position of the current axis the deflections in Leads I, IA, and IP were very small so that the calculated axis was nearly perpendicular to these leads.

For both horizontal and vertical current flow, the deflections in Lead III were larger than those in Lead II and the deflections in Lead aV_L were larger than those in Lead aV_R. It is apparent, therefore, that the differences between the true situation existing in this experiment and that which Einthoven and his associates postulated should be attributed to the eccentric position of the input electrodes. These were placed to the left of the midsternal line, and the left shoulder, being closer to the source of the field than the right, displayed larger potential variations than its fellow.

The methods devised by Burger and Van Milaan[4] make it possible to present practically all of the significant data pertaining to Experiment 3,*b* in a single diagram (Fig. 3). They regard the deflection in a given lead as the scalar product of two vectors, one of which represents that lead and the other the electromotive force responsible for the field. In the Gibb's notation the scalar, or dot, product

of two vectors, **A** and **B**, is written **A·B** in clarendon type. The value of this expression is obtained by multiplying the product of the lengths of the two vectors by the cosine of the angle between the positive direction of the one and the positive direction of the other. This amounts to the same thing as multiplying the length of one vector by the projection of the other upon it. When one vector is of unit length the scalar product is equal to the length of the other multiplied by the cosine of the angle between the directions which the two vectors define.



	H	V
I	38.0	-20.0
II	12.0	38.5
III	-24.0	57.0

	H	V
I_A	26.0	-21.5
II_A	9.5	48.0
III_A	-17.5	67.0
I_P	19.0	-10.0
II_P	5.5	37.0
III_P	-13.5	48.0
RR	4.5	6.0
LL	-3.0	16.0
FF	0.3	-3.0
$(V_T)_P-(V_T)_A$	0.6	6.3

Fig. 3.—Experiment 3, *b*. Diagrams, constructed by the method of Burger and Van Milaan,[4] which depict in graphic form the material shown in Figs. 2, *A* and 2, *B* and in Table I.

In the present discussion we need not be concerned with the absolute, but only with the relative lengths of the vectors with which we shall have to deal. We may, therefore, consider that one which represents the electromotive force as of unit length. When this is done the deflection in any lead is the product of the length of that lead and the cosine of the angle which its positive direction makes with that of the current axis. The problem of finding the vectors which depict the leads used in our experiment then becomes a relatively simple one, for we know for each of these leads the size of the deflections both when the current axis was horizontal and when it was vertical. In the one case the unit vector points from right to left (0 degrees) and in the other it points straight down (90 degrees). The direction of Lead I, for example, with respect to the first of these unit vectors, is defined by the angle of which the tangent is equal to $(I)_V$ divided by $(I)_H$, or $-20/38$ (Table I). Performing the indicated operation, we obtain the figure -0.5263, and on consulting a table of the natural trigonometric functions find that the angle sought is approximately -28 degrees. The length of Lead I, which gives the size of the deflection in this lead, when the

current axis is parallel to it and may, therefore, be represented by the symbol $(E)_I$, can be found by adding the squares of $(I)_V$ and $(I)_H$ and extracting the square root of the sum thus obtained. In the present instance this calculation gives the figure 42.94. Table II gives the length and direction with respect to the horizontal of each of the twelve leads used in the experiment under consideration.

TABLE II. LENGTH AND DIRECTION, WITH RESPECT TO THE HORIZONTAL, OF THE TWELVE LEADS USED

LEAD	LENGTH	ANGLE (DEGREES)
I	42.9	−28
II	40.3	73
III	64.0	114
IA	33.7	−40
IIA	47.0	78
IIIA	70.0	103
IP	21.5	−28
IIP	37.0	81
IIIP	50.0	109
RR	7.5	53
LL	16.3	101
FF	3.0	−84

The rather tedious computations involved in this method can be avoided by the use of a straightedge, square, and ruler. To construct a given lead, proceed as follows: On a horizontal line lay off a segment of a length equal to the amplitude of the deflection for a horizontal input. If this deflection is positive, draw a vertical line through the right, and if it is negative, through the left end of this segment. On this vertical line measure from the horizontal line a length equal to the amplitude of the deflection for a vertical input. This second segment should extend downward when this deflection is positive, and upward when it is negative. Draw the hypotenuse of the right triangle of which these two segments are the perpendicular sides. This line represents the lead vector and its positive direction is from the beginning of its horizontal to the end of its vertical component.

In constructing a diagram such as that shown in Fig. 3, it is, of course, necessary to find only those lead vectors that are independent. When the lead vectors already drawn are sufficient to locate all the electrodes, the others can be found by drawing lines between the points representing the electrodes which they connect.

The augmented unipolar limb leads are represented by the medians of the triangle corresponding to the standard limb leads. The unaugmented unipolar limb leads are those segments of these medians lying between their intersection and the apices of the triangle. The medians of the anterior and the posterior triangle have a similar significance. The vector drawn from the intersection of the medians of the former to the intersection of the medians of the latter depicts a lead from the central terminal of the first to that of the second.

To avoid a possible misunderstanding it should be emphasized that the nine lead diagram of Fig. 3 is not an attempt to reproduce a three dimensional figure upon a flat surface. The sagittal leads RR, LL, and FF appear in this diagram only because they showed deflections when the current axis was parallel to the frontal plane. In other words, these leads had components in the frontal plane, and it is these that appear in the diagram. The sagittal components of these leads, by virtue of which they displayed deflections when the current axis was parallel to the sagittal plane, are not shown.

When the deflections in two of the three leads of an oblique triangle are known, the direction and length of the vector which represents the electromotive force acting can be found. The method of doing this is somewhat different from that employed in the case of an equilateral triangle and requires some words of explanation.

The scalar product of two vectors, **A** and **B**, is equal to the sum of the scalar products obtained by multiplying each of the mutually perpendicular components of the one by the corresponding component of the other; that is, $\mathbf{A}\cdot\mathbf{B} = a_1b_1 + a_2b_2$, where a_1 is the length of the horizontal component of **A**, b_1 is the length of the horizontal component of **B**, and a_2 and b_2 are the lengths of the vertical components of **A** and **B**, respectively.

Let us assume that Leads I and II are those for which the deflections are known. Let D_I and D_{II} stand for these known deflections, and X and Y for the horizontal and vertical components of the unknown electromotive force. We may then form the following equations:

$$(11)\quad D_I = (I)_H X + (I)_V Y$$

$$(12)\quad D_{II} = (II)_H X + (II)_V Y$$

The second member of each of these equations is the sum of the product of the horizontal components of the lead vector and the electromotive force and the product of their vertical components. These equations can easily be solved for the unknowns, X and Y. If the first is divided by the length of Lead I and the second by the length E_{II} of Lead II, we obtain:

$$(13)\quad \frac{D_I}{E_I} = \frac{(I)_H X}{E_I} + \frac{(I)_V Y}{E_I}$$

$$(14)\quad \frac{D_{II}}{E_{II}} = \frac{(II)_H X}{E_{II}} - \frac{(II)_V Y}{E_{II}}$$

These last equations show that the deflection in a given lead divided by its length is equal to the sum of the projections of the horizontal and vertical components of the electromotive force, and, therefore, to the projection of this force as a whole upon that lead. In obtaining the magnitude and direction of the electromotive force graphically, the procedure in the case of the Burger triangle differs from that employed in the case of the Einthoven triangle in only one respect. The former does not have sides that are equal in length and each of the known deflections must be divided by the length of the lead to which it belongs before operations are begun.

EFFECT OF THE POSITION OF THE INPUT ELECTRODES WITH REFERENCE TO THE MIDLINE UPON THE FORM OF THE BURGER TRIANGLE

Five experiments were performed upon Subject 4 and these are designated by the symbols 4,*b*, 4,*c*, 4,*d*, 4,*e*, and 4,*f*. In all these experiments the input electrodes (1.1 cm. in diameter) were at the same vertical level (fourth intercostal space at the sternal margin) and the current passed through them was 0.5 milliamperes. In three instances they were 5.0 cm. apart (4,*b*, 4,*d*, and 4,*f*); in the first of these, the point midway between them was 5.0 cm. to the right of the mid-

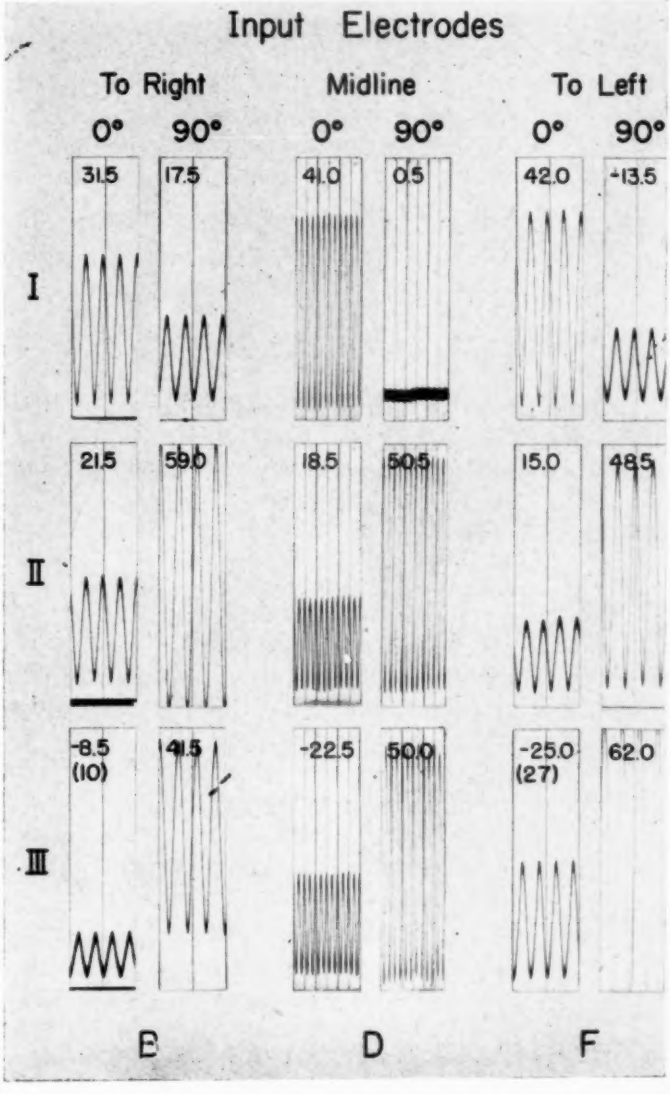


Fig. 4.—Experiments 4, *b*, 4, *d*, and 4, *f*. Input electrodes to the right of the midline in 4, *b*, in the midline in 4, *d*, and to the left of the midline in 4, *f*. The deflections in the standard limb leads when the current axis was horizontal (0°) and when it was vertical (90°).

sternal line, in the second it was on this line, and in the third it was 5.0 cm. to the left of it. The tracings obtained in these three experiments when the current axis was horizontal and when it was vertical are reproduced in Fig. 4, and the corresponding triangles are shown in Fig. 5. Experiments 4,*c* and 4,*e* were identical with Experiments 4,*b* and 4,*d*, respectively, except that the distance between

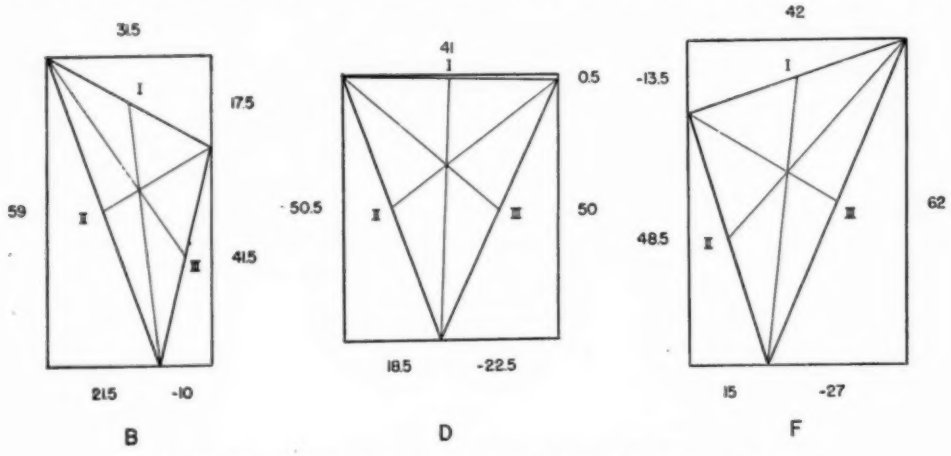


Fig. 5.—The Burger triangles corresponding to the deflections shown in Fig. 4.

the input electrodes was 2.0 cm. instead of 5.0 centimeters. The effects of this reduction in the electrical moment are summarized in Table III, which gives for all of the five experiments the amplitudes of the deflections in the limb leads for two positions of the current axis, the length (E_I, E_{II}, etc.) of each lead vector, and the angle between it and the horizontal.

TABLE III. EFFECT OF REDUCTION OF DISTANCE BETWEEN INPUT ELECTRODES (ELECTRICAL MOMENT)

EXPERIMENT	INPUT ELECTRODES		DEFLECTIONS					
	POSITION	DISTANCE APART	LEAD I		LEAD II		LEAD III	
			0 H	90 V	0 H	90 V	0 H	90 V
4b	5 cm. right	5 cm.	31.5	17.5	21.5	59.0	−8.5	42.0
4c	5 cm. right	2 cm.	15.5	8.0	10.5	25.0	−4.5	15.5
4d	Midline	5 cm.	41.0	0.5	18.5	50.5	−21.5	50.0
4e	Midline	2 cm.	22.5	0.5	10.0	21.0	−12.5	20.5
4f	5 cm. left	5 cm.	42.0	−13.5	15.0	48.5	−25.0	62.0
			E_I	ANGLE (DEGREES)	E_{II}	ANGLE (DEGREES)	E_{III}	ANGLE (DEGREES)
4b	5 cm. right	5 cm.	36.0	29	62.8	70	43.2	103
4c	5 cm. right	2 cm.	17.6	27	27.1	67	16.1	106
4d	Midline	5 cm.	41.0	0	53.3	70	54.4	114
4e	Midline	2 cm.	22.5	0	23.2	65	23.9	121
4f	5 cm. left	5 cm.	44.1	−18	50.8	73	67.3	113

It is of interest that when we reduced the distance between the input electrodes from 5.0 to 2.0 cm., without altering the size of the current flowing, the amplitude of the deflections fell somewhat more than 50 per cent, on the average, but the shape of the Burger triangle did not materially change.

When the point midway between the centers of the electrodes was on the midsternal line, the triangle was isosceles, or very nearly so, with the side corresponding to Lead I shorter than those corresponding to Leads II and III. When this point was to the right of the midline, Lead II was longer than Lead III and the angle which defines the direction of Lead I was positive; when it was to the left of the midline, Lead III was larger than Lead II and the angle between Lead I and the horizontal was negative. There can be no doubt that in the first of these three cases the potential variations of the two arms were of approximately the same magnitude. In the second the potential variations of the right arm were greater than those of the left for both positions of the current axis; in the third the reverse was true.

ON SEPARATING THE HORIZONTAL AND VERTICAL COMPONENTS OF THE FIELD AND BRINGING THE POTENTIAL OF THE CENTRAL TERMINAL TO ZERO

In Experiment 4,*d* the Burger triangle was very close to isosceles (Fig. 5). Let us make it exactly so by equalizing the absolute magnitudes of the deflections in Leads II and III; this process gives for the amplitudes of the deflections in the various leads the following figures:

$(I)_H$	$(II)_H$	$(III)_H$	$(V_R)_H$	$(V_L)_H$	$(V_F)_H$
41.0	20.5	−20.5	−20.5	20.5	0
$(I)_V$	$(II)_V$	$(III)_V$	$(V_R)_V$	$(V_L)_V$	$(V_F)_V$
0	50.3	50.3	−16.7	−16.7	33.4

In this case, it is clearly possible to separate the horizontal and the vertical components of the electromotive force, for the purpose, for example, of obtaining an accurate vectorcardiogram. Lead I yields a deflection of 41 mm. when the current axis is horizontal and no deflection when this axis is vertical. Lead V_F gives a deflection of 33.4 mm. when the current axis is vertical and no deflection when it is horizontal. By recording Lead I with the "horizontal channel" of the vectorcardiograph operating at its "normal" sensitivity, and Lead V_F simultaneously with the "vertical channel" of the vectorcardiograph operating at a sensitivity 41/33.4 times as great, we should obtain an accurate record of the changes in the position of the electrical axis.

When the current axis was horizontal the deflection in Lead V_F was zero; that is, the central terminal and the left leg were at the same potential. The spatial relations between the input electrodes and the junctions of the limbs with the trunk were such that there can be no doubt that this potential was zero in the sense that it was midway between that of the region where the current entered and that of the region where the current left the body. On the other hand, the shape of the Burger triangle indicates that when the current axis was vertical the potential of the central terminal was not zero in this sense. It may seem

probable that the shape and dimensions of the triangle, which are given, supply the data necessary for the computation of the potential of this terminal, but this is not the case, unless it be assumed that the point midway between the input electrodes was "electrically" equidistant from the limb electrodes. Actually, this point was much farther, in the geometric sense, from the junction of the left leg with the trunk than from the junctions of the arms with the trunk. The assumption mentioned amounts to the supposition that the field in this experiment was equivalent to that of a centric dipole in a homogeneous conducting sphere. In the case of a model of this kind, and leads from electrodes that are equidistant from the center of the homogeneous spherical volume conductor, the Burger triangle and the geometric triangle defined by the three lead electrodes are similar in the technical Euclidean sense; each side of the one is parallel to the corresponding side of the other. Under the circumstances specified, the same statement holds for other figures, including the Burger tetrahedron and the corresponding geometric tetrahedron defined by four lead electrodes not all in the same plane. Under all other circumstances, the Burger triangle or tetrahedron, as the case may be, differs in shape from the geometric triangle or tetrahedron of which the lead electrodes are the apices.

If we make the assumption in question, the potential of the central terminal when the current axis was vertical can be found in the following way: The tangent of half the angle at that apex of the isosceles triangle corresponding to the leg electrode is given by the ratio $\frac{{}^{1}/_{2}(I)_H}{(II)_V}$, or $\frac{20.5}{50.3}$, which is equal to 0.4075. This is the tangent of 22 degrees. Knowing this angle, we can find the other angles of the triangle. The angle made with the horizontal by the radius vector from the center of the circle defined by the apices of the triangle to that apex which corresponds to the electrode on the left arm is 90 degrees minus 44 degrees, or 46 degrees. The true potential of this electrode when the current axis was vertical was, therefore, R sin -46 degrees where R is the radius of the circle mentioned and therefore the length of the leads from the center of this circle to the apices of the triangle. Since the true potential of the leg electrode was consequently R cos 0 degrees when the current axis was vertical, we have the equation

$$R \cos 0^\circ - R \sin -46^\circ = (II)_V$$

or

$$R(1 + 0.695) = 50.3, \text{ and } R = 29.7$$

The true potential of the left leg was then 29.7 tenths of a millivolt and the true potential of the central terminal 29.7 minus 33.4 or -3.7 tenths of a millivolt. We have carried out this computation for the sake of introducing the problem of reducing the potential variations of the central terminal to zero. We do not believe that the assumption on which it is founded is valid.

In a preceding section of this paper, it was pointed out that the vectors drawn from the intersection of the medians of the Burger triangle to its apices represent the three unaugmented unipolar limb leads. Since these leads measure the potential of the limb electrodes with respect to that of the central terminal, we may consider each apex of this triangle at the same potential as the correspond-

ing extremity. We may likewise regard the intersection of the medians as at the same potential as a central terminal connected to the limb electrodes through equal resistances. With the midpoint of each side of the triangle we may associate a potential half-way between the potentials of the apices it connects. We may suppose that along each side and each median of the triangle the potential falls uniformly from the end of that side or median where it is higher to the end where it is lower. Every point inside the triangle is then at a potential which may be regarded as a weighted mean of the potentials of its apices. When the dipole responsible for the field and the lead electrodes lie in the same plane and the dipole is inside the geometric triangle which these electrodes define, one of the points of the corresponding Burger triangle is at zero potential for every position of the dipole axis. When the dipole is outside the electrode triangle it is clear that all of its apices, and, consequently, all points inside the Burger triangle, must be positive for some positions of the electrical axis and negative for others.

When the resistances in the arms of the central terminal are equal, its potential is the mean of the potentials of the apices of the triangle. By making these resistances unequal and giving them the proper relative magnitude, it is, however, possible to make the potential of the central terminal equal to that of any point on the perimeter of the triangle or inside it. We may regard CR, CL, and CF leads as leads from a central terminal connected to two apices of the triangle by infinite resistances. In this case, the potential of the terminal is the same as that of the third apex. Augmented unipolar limb leads are leads from a central terminal with equal resistances in two of its branches and an infinite resistance in the third. In this case, the reference potential is that of the midpoint of one of the sides of the triangle. By varying one of the three resistances without altering the other two, we can make this potential equal to that of any point lying on the median which runs from the apex corresponding to the altered resistance to the midpoint of the opposite side. The same result is obtained by leaving this resistance unchanged and altering the other two in equal measure. By making one resistance infinite and varying one of the others, we can give the central terminal a potential equal to that of any point on the side of the triangle opposite to the apex that has been disconnected. By making unequal changes in two of the three resistances, we can shift the potential of the terminal to that of any point lying inside any of the circumscribed areas into which the medians divide the triangle.

The change in the potential of the central terminal effected by a specified alteration of the relative magnitudes of the resistances in its three branches may be computed in the following way: Consider the equations:

$$(15)\quad 1/r_a\,(V_R - V_T^1) = i_a$$
$$(16)\quad 1/r_b\,(V_L - V_T^1) = i_b$$
$$(17)\quad 1/r_c\,(V_F - V_T^1) = i_c$$

in which r_a, r_b, and r_c are the resistances between the central terminal and the junctions with the trunk of the right arm, left arm, and left leg, respectively; V_T^1 is the potential of this terminal when these resistances are unequal; V_R, V_L, and V_F are the open circuit potentials of the three extremities; and i_a, i_b, and i_c

are the currents flowing toward the central terminal through the corresponding resistances. By Kirchhoff's current law, the sum of these three currents is zero, and if we add Equations 15, 16, and 17 and multiply by $r_a r_b r_c$, we obtain the expressions:

$$(18)\quad r_b r_c (V_R - V_T^1) + r_a r_c (V_L - V_T^1) + r_a r_b (V_F - V_T^1) = 0$$

and

$$(19)\quad V_T^1 = \frac{r_b r_c V_R + r_a r_c V_L + r_a r_b V_F}{r_b r_c + r_a r_c + r_a r_b}$$

When the three resistances are equal the potential of the central terminal, (V_T) is given by:

$$(20)\quad V_T = \frac{V_R + V_L + V_F}{3}$$

and

$$(21)\quad V_T^1 - V_T = \frac{r_b r_c (V_R - V_T) + r_a r_c (V_L - V_T) + r_a r_b (V_F - V_T)}{r_b r_c + r_a r_c + r_a r_b}$$

Since

$$(22)\quad r_a r_b (V_F - V_T) = -r_a r_b (V_R - V_T) - r_a r_b (V_L - V_T)$$

it follows that

$$(23)\quad V_T^1 - V_T = \frac{r_b (r_c - r_a) (V_R - V_T) + r_a (r_c - r_b) (V_L - V_T)}{r_b r_c + r_a r_c + r_a r_b}$$

$$(24)\quad V_T^1 - V_T = \frac{\left(\frac{r_c}{r_a} - 1\right) (V_R - V_T) + \left(\frac{r_c}{r_b} - 1\right) (V_L - V_T)}{\frac{r_c}{r_a} + \frac{r_c}{r_b} + 1}$$

It is convenient to have also expressions for the currents i_a, i_b, and i_c in terms of the open circuit voltages (I), (II), and (III) in the three limb leads and the resistances r_a, r_b, and r_c. For certain purposes the internal resistances between the junctions of the extremities with the trunk must be considered. We shall here regard these as equal and small in comparison with the external resistances (r_a, r_b, and r_c) and represent them by the symbol r_1. The expressions referred to are given in a previous paper from this laboratory.[5] The currents mentioned appear in them as fractions with the denominator

$$(25)\quad r_1^2 + 2r_1 (r_a + r_b + r_c) + 3 (r_a r_b + r_a r_c + r_b r_c)$$

Representing this denominator by k we have:

$$(26)\quad ki_a = -(r_1 + 3r_c) (I) - (r_1 + 3r_b) (III)$$
$$(27)\quad ki_b = (r_1 + 3r_c) (I) - (r_1 + 3r_a) (II)$$
$$(28)\quad ki_c = (r_1 + 3r_b) (II) + (r_1 + 3r_a) (III)$$

Equation 19 is true for all positions of the current axis and all values of V_T', including the value zero. Consequently,

$$(29)\quad r_b r_c\,(V_R)_H + r_a r_c\,(V_L)_H + r_a r_b\,(V_F)_H = 0$$

$$(30)\quad r_b r_c\,(V_R)_V + r_a r_c\,(V_L)_V + r_a r_b\,(V_F)_V = 0$$

These equations may be solved for the ratios r_a/r_c, r_b/r_c, and r_b/r_a, the last of which is the second divided by the first.

$$(31)\quad \frac{r_a}{r_c} = \frac{(V_R)_V(V_L)_H - (V_R)_H(V_L)_V}{(V_F)_H(V_L)_V - (V_F)_V(V_L)_H}$$

$$(32)\quad \frac{r_b}{r_c} = \frac{(V_L)_V(V_R)_H - (V_L)_H(V_R)_V}{(V_F)_H(V_R)_V - (V_F)_V(V_R)_H}$$

$$(33)\quad \frac{r_b}{r_a} = \frac{(V_F)_V(V_L)_H - (V_F)_H(V_L)_V}{(V_F)_H(V_R)_V - (V_F)_V(V_R)_H}$$

These are the relative magnitudes of the resistances required to bring the potential of the central terminal to zero when the true potentials of the limb electrodes are known for two positions of the current axis, provided that the dipole is inside the triangle.

When this triangle is isosceles $(V_F)_H$ is zero and Equation 33 gives

$$(34)\quad \frac{r_b}{r_a} = \frac{(V_L)_H}{-(V_R)_H} = \frac{-(III)_H}{(II)_H} = 1$$

and, since $(V_R)_V$ and $(V_L)_V$ are equal and $-(V_R)_H$ and $(V_L)_H$ are equal, Equations 31 and 32 give

$$(35)\quad \frac{r_a}{r_c} = \frac{2(V_R)_V}{(V_F)_V}$$

and

$$(36)\quad \frac{r_b}{r_c} = \frac{2(V_L)_V}{(V_F)_V}$$

These last equations are true not only when the triangle is isosceles, but also whenever $(V_F)_H$ is zero and $\dfrac{(V_R)_V}{(V_L)_V}$ is equal to $\dfrac{-(V_R)_H}{(V_L)_H}$; that is, whenever the lead vector V_F is parallel to the vertical axis and the angles made with this axis by the lead vectors V_R and V_L are equal.

We may now turn to a consideration of the triangles (Fig. 5) corresponding to Experiments 4,*b*, 4,*d*, and 4,*f*. For the last, we have for the deflections in the standard and unaugmented limb leads the following figures:

$(I)_H$	$(II)_H$	$(III)_H$	$(V_R)_H$	$(V_L)_H$	$(V_F)_H$
42.0	15.0	−27.0	−19.0	23.0	−4.0
$(I)_V$	$(II)_V$	$(III)_V$	$(V_R)_V$	$(V_L)_H$	$(V_F)_V$
−13.5	48.5	62.0	−11.7	−25.2	36.8

In this experiment, there were deflections in all of the leads used, both when the current axis was horizontal and when it was vertical. In cases of this kind, it is possible to alter the ratio r_b/r_a in such a way as to make the potential of the central terminal and that of the leg electrode equal when the current axis is horizontal. When these two potentials are equal the current i_c is zero.

According to Equation 28 we have, when *ic* is zero,

$$(37)\quad \frac{r_1 + 3r_b}{r_1 + 3r_a} = \frac{-(III)_H}{(II)_H}$$

or, when r_1 is neglected as negligibly small in comparison with $3r_a$ and $3r_b$,

$$(38)\quad \frac{r_b}{r_a} = \frac{-(III)_H}{(II)_H}$$

In the present instance, this equation gives for the magnitude of the ratio sought the figure 27/15, or 1.8. The result of the indicated alteration of the relative magnitude of the resistances involved would be to make the potential of the central terminal 4 units less positive and to reduce $(V_F)_H$ to zero. The horizontal component of the dipole would then produce no deflection in Lead V_F, and the deflection in this lead would be proportional to the vertical component. This procedure can be carried out whenever the deflection in Lead I, when the current axis is horizontal, is larger than the deflection in either of the other two limb leads. Under certain circumstances, it is possible to obtain a second lead which will yield a deflection proportional to the horizontal component of the dipole and no deflection for the vertical component by altering the ratios r_a/r_c and r_b/r_c in the manner required to make the currents i_a and i_b equal when the current axis is vertical. When the ratio i_b/i_a equals 1 we have from Equations 26 and 27 when the resistance r_1 is neglected

$$(39)\quad r_c\,(I)_V - r_a\,(III)_V = -r_c\,(I)_V - r_b\,(II)_V$$

$$(40)\quad \frac{r_a}{r_c} = \frac{-2(I)_V}{\frac{r_b}{r_a}(II)_V - (III)_V}$$

By substituting in this equation the values −13.5, 48.5, and 62 given for the deflections in Leads I, II, and III, respectively, when the current axis was vertical and the value 1.8 found for the ratio r_b/r_a, we obtain for r_a/r_c the value 1.067, and for the ratio r_b/r_c the value 1.92. A central terminal connected to the limb electrodes by resistances having these relative magnitudes would be 4 units less positive when the current axis was horizontal and 5.2 units less negative when this axis was vertical than a central terminal connected to these electrodes through equal resistances. Whenever i_a and i_b are equal, when the current axis is vertical, a lead from any point on the right-arm resistor to a point on the left-arm resistor, which is separated from the central terminal by the same resistance, will yield a deflection proportional to the horizontal component of the electromotive force; its vertical component will give rise to no potential difference between such points. In the present instance, the potentials with respect to the central terminal of the three points on its arms separated from it by a resistance equal to r_c have been computed for the two positions of the current axis. For a horizontal current axis, the figures are −15.0, 15.0, and 0, and for a vertical current axis they are −16.9, −16.9, and 33.8 for the points on the right arm, left arm, and leg resistor, respectively.

For the other experiments that have been referred to in this paper, the values of the ratios of the resistances in the arms of the central terminal required to make i_c zero when the current axis was horizontal, and i_a equal to i_b when this axis was vertical are as follows: for Experiment 4,*b*, r_a/r_b equals 2.2, r_a/r_c equals 2.5, and r_b/r_c equals 1.2; for Experiment 4,*c* the corresponding figures are 2.1, 3.1, and 1.5, respectively. For Experiment 3,*b* the values are r_b/r_a equals 2.2, r_b/r_c equals 3.5, and r_a/r_c equals 1.6. In all of these experiments, it would, therefore, have been possible to separate the horizontal and vertical components of the electromotive force for any position of the electrical axis by the methods proposed.

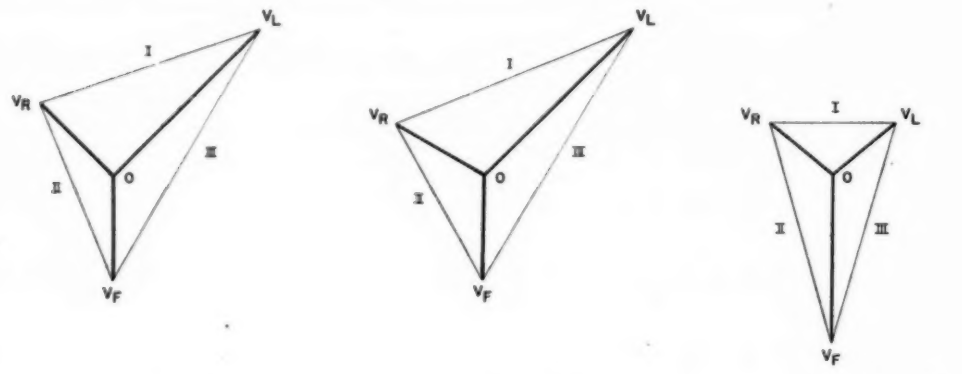
In order to make clear the limitations of these methods and the kind of cases in which they are applicable, we may consider three hypothetical triangles (Fig. 6). The values assumed for the true potentials of the three electrodes are for each of these triangles, as follows:

Triangle	$(V_R)_H$	$(V_L)_H$	$(V_F)_H$	$(V_R)_V$	$(V_L)_V$	$(V_F)_V$
(A)	−2.12k	4.24k	0	−2.12k	−4.24k	3k
(B)	−2.60k	4.24k	0	−1.5k	−4.24k	3k
(C)	−1.865k	1.865k	0	−1.506k	−1.506k	4.888k

The letter k is an arbitrary constant.

In the first case (A) the field is that of a centric dipole in a homogeneous medium. The angles between the radius vectors to the R and L apices of the triangle and the negative one-half of the vertical axis are both 45 degrees. The electrode at the first of these apices is on the surface of the medium, as is also the electrode at the F apex. The other electrode is enough closer to the centric dipole to make its potential variations twice as large as they would be if it too

were on this surface. The radius vector to the F electrode makes an angle of 0 degrees with the positive direction of the vertical axis. The methods described give for the ratios of the resistances in the arms of the central terminal the values r_b/r_a equals 2, r_a/r_c equals 1.414, r_b/r_c equals 2.828. These are the values required to reduce the potential of the central terminal to zero.



	H	V
V_R	-2.12	-2.12
V_L	4.24	-4.24
V_F	0	3.00

A

	H	V
V_R	-2.60	-1.50
V_L	4.24	-4.24
V_F	0	3.00

B

	H	V
V_R	-1.87	-1.51
V_L	1.87	-1.51
V_F	0	4.88

C

Fig. 6.—Three hypothetical Burger triangles. (See text.)

In the second case (B), the field is again that of a centric dipole in a homogeneous spherical medium and the L electrode is in the same position as in Case (A); it is not at the surface of this medium as are the other two. The radius vector to the R apex makes an angle of 60 and that to the L apex an angle of 45 degrees with the negative direction of the vertical axis. The radius vector to the F apex again makes an angle of zero degrees with the positive direction of this axis. In this instance, the value of r_b/r_a required, when the current axis is horizontal, to make the potential of the central terminal and the current i_c zero is 1.633, and this is equal to $\frac{-(III)_H}{(II)_H}$, or $\frac{4.24}{2.60}$. On the other hand, the values of r_a/r_c and r_b/r_c required to make i_a and i_b equal, when the current axis is vertical, are 51.8 and 84.6, respectively. It is clearly not feasible to equalize these currents in cases of this kind. The values of r_a/r_c and r_b/r_c required to make the potential of the central terminal zero for a vertical current axis are 1.366 and 2.231, respectively. These are the values which make the ratio i_b/i_a equal to the ratio of minus tangent Θ_2 to tangent Θ_1, where Θ_2 is the angle between the positive direction of the horizontal axis and the radius vector to the L apex, and Θ_1 the corresponding angle between this axis and the radius vector to the R apex of the triangle. It is, nevertheless, possible to find in this instance a lead

from a point on the right arm resistor to a point on the left arm resistor which will give a deflection proportional to the horizontal component of the dipole and no deflection in response to its vertical component. It is clear that this can be done whenever the arm electrodes are both strongly negative with respect to the central terminal, for the currents i_b and i_a then have the same sign. If the point on the right arm resistor is separated from the central terminal by the resistance A and that on the left arm resistor is separated from this terminal by the resistance B, the two points will be at the same potential provided Ai_a is equal to Bi_b and this condition can always be fulfilled by choosing the two points properly. In the third case (C), all three electrodes are on the surface of the spherical medium and at the apices of an equilateral triangle. The dipole is at a point on the radius vector to the F electrode at a distance from the center of the sphere equal to one-fourth of its radius. In computing the potentials of the apices of the equilateral triangle in this hypothetical case, we have utilized equations for the field of an eccentric dipole in a spherical medium which were developed by Wilson and Bayley.[5] The Burger triangle is isosceles and of the type in which the side corresponding to Lead I is shorter than those corresponding to Leads II and III. Its shape is, therefore, similar to that of the isosceles triangle of Fig. 5. It does not tell us whether the dipole is centric and the geometric triangle defined by the electrodes therefore identical with it in form, or whether the dipole is eccentric and this geometric triangle equilateral, or isosceles but different from it in shape. The assumption that the dipole is centric leads to the conclusion that the potential of the F electrode for a vertical current axis is 3.47k, whereas its true potential is 4.88k, and that the potential of the central terminal is -0.79k instead of 0.63k which is correct. In summing up this section, we may say that in experiments of the kind under consideration, it is always possible to find one lead which will record only the variations of the horizontal, and another which will record only the variations of the vertical component of the electrical field. It is always theoretically possible to modify the relative magnitude of the resistances in the arms of a central terminal connected to the three limb electrodes in such a way as to insure that its potential will be zero for all positions of the electrical axis, provided that the position of the input electrodes is not one that will make all three lead electrodes simultaneously positive or negative. On the other hand, it is not practically possible to do this unless the true potentials of the limb electrodes are known for two positions of the current axis. It does not appear that this necessary information can be obtained in any way other than by measuring the potentials of these electrodes with reference to that of some point possessing, in respect to the circumscribed region where the current enters the body, "electric" and spatial relations identical with those which it bears to the circumscribed region where the current leaves the body. For some positions of the input electrodes it may be that no point which precisely fulfills the prescribed conditions exists. In that case, it may even be difficult to define in a manner satisfactory to everyone exactly what is meant by zero potential in that particular instance. The concept is one that is derived from the consideration of hypothetical situations for which exact mathematical solutions are available. In practice, the solution of the problem of finding a point at zero

potential represents an approximation to an ideal based on plausible assumptions of one kind or another. We have as yet made no serious attempt in our experiments to measure the potentials of the limb electrodes with respect to that of a point of the kind mentioned, and shall not now discuss this problem further.

In the title of this article, we have referred to the possibility of constructing an Einthoven triangle for a given subject. In order to do this, it would be necessary to be able to generate in the trunk of the given subject an electrical field closely resembling that associated with the heart beat, and to measure the induced potential differences between the limb electrodes for two different positions of the electrical axis. By the method of Burger and Van Milaan, a triangle corresponding to the data thus obtained could then be constructed.

The extent to which the electrical field set up in the body by connecting two electrodes on the precordium to a source of low frequency alternating current resembles the electrical field of the heart is as yet unknown. It may be possible to generate an artificial field in the trunk more like that of the heart by placing small input electrodes in the esophagus or by introducing them into the right ventricle by the catheterization technique. Since the stimulating effect of the current increases rapidly with the current density, the size of the current that could be safely passed into the body by way of the largest input electrodes permissible in such experiments might be inconveniently small, but with a sufficiently sensitive recording system the field produced could undoubtedly be studied satisfactorily. Much information bearing on the problem of generating an artificial field similar to the cardiac field will certainly come from a comparison of the results of experiments on living subjects with those obtained in like experiments on cadavers and on models.

Human chests differ in size and shape and human hearts in location, but we do not as yet have much information concerning the effects of these variations upon the character of the heart's electrical field. In the majority of our experiments in which the point midway between the input electrodes was on the midsternal line and at the level of the fourth intercostal space, the Burger triangle was very nearly isosceles and of the kind in which the side corresponding to Lead I was shorter than the sides corresponding to Leads II and III. In two instances, however, this triangle was of the opposite type. We do not know whether the shape of the triangle obtained was dependent upon the size and shape of the chest or upon some other factor. A larger series of experiments should decide this question.

THREE ISOPOTENTIAL LINES AND THE RECIPROCITY THEOREM OF HELMHOLTZ

In a preceding section of this paper, it was mentioned that we have carried out a very few experiments of a kind suggested by Dr. Kenneth S. Cole, in which two of the limb electrodes are connected to a current source and the isopotential line corresponding to the potential of the third limb electrode is plotted on the body surface. The three lines obtained in this way may be called the right arm isopotential, the left arm isopotential, and the leg isopotential. They intersect at two points, one on the anterior and the other on the posterior surface of the

chest. In the experiments performed thus far, the anterior point has been very close to the midsternal line and usually at the level of the sternal attachment of the fourth costal cartilage or the fourth intercostal space. In the case of one subject, however, it was at the level of the second intercostal space. In the single experiment in which it was located, the posterior point was directly behind the anterior. The isopotential lines found in this instance are shown in Fig. 7.

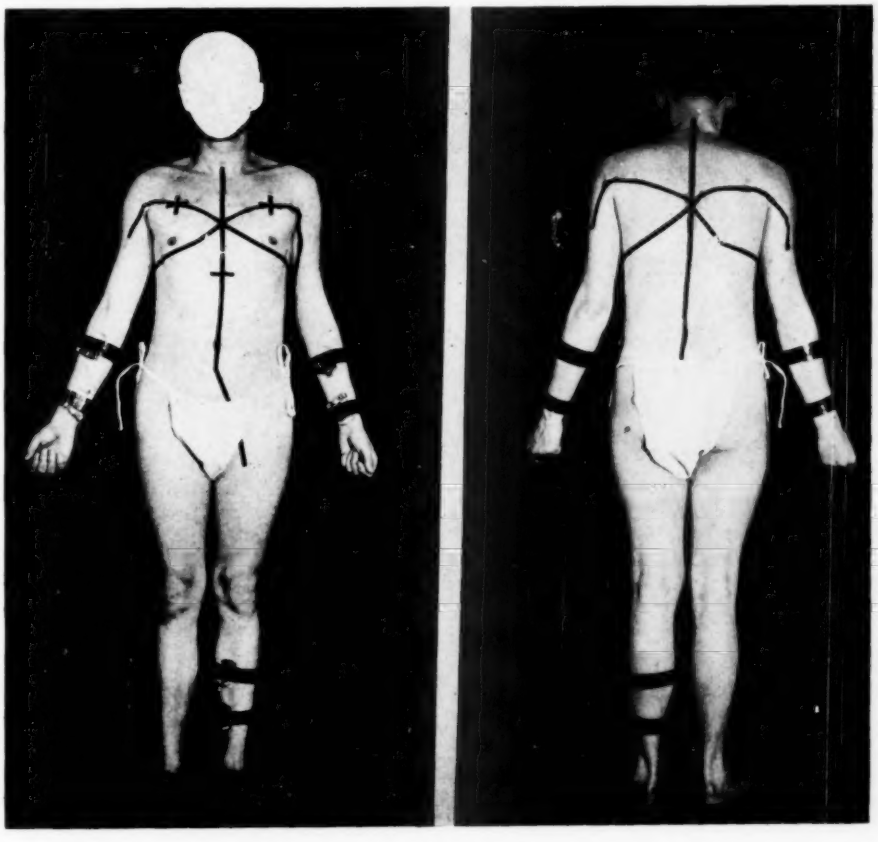


Fig. 7.—Experiment 12. The location of the anterior and posterior intersections of the right arm, left arm, and leg isopotentials.

In Experiment 12, the input electrodes were placed on the leg isopotential at the level required to make the point midway between them and the anterior intersection of the three isopotential lines coincide. The resulting deflection in Lead I was very small and a slight rotation of the input electrodes made it disappear altogether. The wires from the oscillator were then transferred to the electrodes on the arms and the lead wires to the electrodes on the chest. The record obtained again showed no deflection. This procedure was repeated after rotating the current axis through an angle of 90 degrees. This axis was then perpendicular to the leg isopotential and the electrodes were equidistant from it. Under these

circumstances, the deflections recorded were of the same size when the oscillator was connected to the chest electrodes and the lead wires to the limb electrodes as when the reverse was the case (Fig. 8). These observations are in accord with the reciprocity theorem. In 1853, Helmholtz,[7] then a young man 32 years of age, proved this theorem theoretically and experimentally for both homogeneous and heterogeneous volume conductors. We believe that the location of the intersections of the three isopotential lines specified will prove to be a very useful procedure. It promises to disclose significant differences between subjects, and since it requires very little time, a large number can be examined in a relatively short period. It will also make it possible in experiments on different subjects to place the input electrodes in such a manner that their positions, from the electrical point of view, will always be the same with respect to the limb electrodes. What is more important, the principles underlying this procedure and the reciprocity theorem suggest a great variety of experiments which may increase our knowledge of the properties of the body considered as a volume conductor of electrical currents of the kind associated with the heart beat.

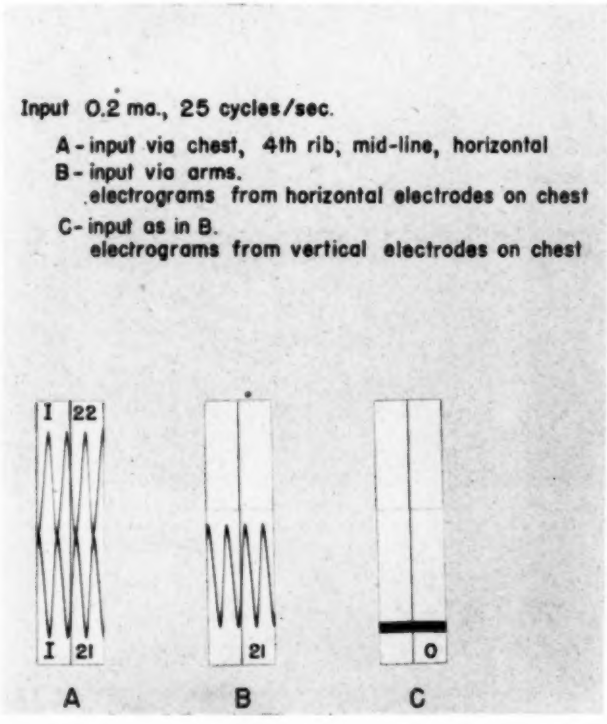


Fig. 8.—Experiment 12. Tracings which illustrate the reciprocity theorem. When there are two electrodes on the limbs and two on the chest, the potential difference between the chest electrodes when the current source was connected to the limb electrodes is equal to the potential difference between the limb electrodes when the current source was connected to the chest electrodes.

THE IMPORTANCE OF THE EFFECTS OF THE POSITION OF THE HEART UPON THE FORM OF THE ELECTROCARDIOGRAM

The ultimate purpose of the work with which this article is concerned is the same as that which led Einthoven and his associates[8] to propose a method of finding the position of the electrical axis of the heart. The first two paragraphs of their famous paper in which this method is described run as follows:

"Die Herzlage beeinflusst die Form des E.K.G. Es ist uns jedoch bei der elektrokardiographischen Untersuchung hauptsächlich darum zu tun, die *Tätigkeit* des Herzens besser zu ermittlen, und man sieht leicht ein, dass, wenn schon durch eine Lageabweichung dieses Organs eine Veränderung in die Form der Kurve hervorgerufen wird, eine Schwierigkeit enstehen muss, um mittels dieser Form auch über die Tätigkeit des Herzens zu urteilen.

Diese Schwierkeit kann am besten gelöst werden, wenn man den Einfluss der Lage vorher genau kennen gelernt hat."

Waller, and many others interested in the electrical aspects of the heart beat, was conscious of this problem long before Einthoven, Fahr, and De Waart attempted to solve it. Today, the differentiation of phenomena produced by displacement or rotation of the heart from those originating within the myocardium itself is still one of the most troublesome of the problems that confront those who attempt to interpret the human electrocardiogram.

There may be little value in computing the exact position of the electrical axis of the heart by Einthoven's method, but there can be no question that the Einthoven triangle has made it possible to recognize with considerable facility peculiarities in the form of the electrocardiogram that result from rotation of the heart about a sagittal axis. The recognition of those peculiarities that result from rotation of the heart about an axis that is not perpendicular to the plane of the limb leads is still extremely difficult. At the same time, our experience with precordial leads has led us to believe that cardiac rotations of this kind are much more often responsible for erroneous interpretations of the electrocardiogram than was formerly suspected. Many changes in the position of the heart that have a profound effect upon the shape of the electrocardiographic deflections cannot at present be recognized by fluoroscopy or by roentgenographic methods. It seems likely, however, that a sound method of taking simultaneously two accurate vectorcardiograms which represent the projections of the cardiac vector upon two different planes and which can be combined to form a spatial curve will contribute heavily to the eventual solution of this important problem. Several methods of this kind have been proposed and some of these have been used to a limited extent. Nevertheless, it has seemed to us that it is desirable to place all methods concerned with the study of the electrical axis of the heart upon a foundation more secure than that upon which they now rest by a thorough experimental study of the distribution in the body of currents similar to those associated with the heart beat. It was with this end in mind that experiments of the kind here reported were undertaken.

SUMMARY

In experiments on normal subjects, two small electrodes on the chest were connected to a source of low frequency current. The resulting differences in potential between the extremities and between other points on the body were measured. By the method described by Burger and Van Milaan, triangles and other figures, which present in graphic form the data obtained in this way, have been constructed.

When the point midway between the input electrodes was in the midsternal line, the triangle corresponding to the standard limb leads was nearly isosceles, and usually, though not always, of the type in which the side corresponding to Lead I was shorter than the other two. When the input electrodes were to the left of the midline, the side of the triangle corresponding to Lead III, and when they were to the right of the midline, the side corresponding to Lead II, was the longest.

When the Burger triangle is oblique, none of the standard or unipolar limb leads yield deflections proportional to either the horizontal or the vertical component of the electrical field. A method of finding two leads, one of which will record the variations of the first of these components, and one which will record the variations of the second, is described. The effect of varying the resistances in the arms of the central terminal upon its potential, and the possibility of reducing the potential variations of this terminal to zero, when the Burger triangle is not equilateral, are discussed.

In a few experiments, the isopotential lines corresponding to the potential of one of the limb electrodes when the other two were connected to a source of low frequency current were plotted on the body surface. The three lines obtained in this way intersect at two points, one on the front and the other on the back of the chest.

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SURGICAL TREATMENT OF HYPERTENSIVE HEART DISEASE AND OF HEART FAILURE OF HYPERTENSION

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DURING the last few years, extensive surgical resection of sympathetic nerves has been gaining importance in the treatment of so-called essential hypertension. There is enough proof of its immediate efficacy, but its later benefits are still under discussion.

After the purely speculative period of Danielopolu and Pende, who suggested the operation, after the heroic period of the pioneers of the method, Peet, Crile, Adson, and many others, who tried the most varied techniques of rhizotomy, sympathectomy, and ganglionectomy, we clinicians remained skeptical or even distrustful, because of the great number of failures.

In the last six years surgery seems to have improved the technique and to have established a method by which results have turned favorable. Ample intervention, both thoracic and abdominal, such as Smithwick's, with resection of great portions of the sympathetic chain, have produced results which were previously thought to be impossible. Today, everywhere, a great number of hypertensive patients are operated upon. They may not be cured, but their blood pressures are lowered and their symptoms at least are improved. Perhaps fatal complications are eliminated or delayed. In any event, operation makes many hypertensive patients capable of returning to normal life and activity.

It is a sure fact that surgical treatment lowers high blood pressure considerably in the majority of cases and that improvement usually lasts for long periods of time. As a natural consequence the excessive strain on the heart is reduced proportionately. Nevertheless, it is wise to review the problem with a critical spirit in order to determine whether surgical intervention is the proper way in which to cure heart failure which is so often a complication in hypertension.

Let us then review the possibilities offered by surgical treatment. It is accepted that patients whose hypertension is slight and responds to medical treatment present no particular problem and are not to be considered for surgery. The problem arises with patients in whom the blood pressure, particularly the diastolic, is very high and in whom medical treatment has proved inefficacious, and particularly with patients in whom severe complications are to be expected.

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This is equivalent to the statement that surgical treatment is limited to the group of patients with severe hypertension. But even in this group selection must be made. Severe arterial degeneration makes improvement after surgery improbable. The same has been said regarding advanced visceral complications, cardiac or renal, especially if these complications have produced organic insufficiency. Likewise, recent cerebral thrombosis or hemorrhage has, up to now, placed a patient beyond the benefit of surgery.

If patients with slight hypertension are eliminated and those with advanced or complicated disease are discarded and surgical treatment, therefore, is limited to an intermediate group in whom intervention can be predicted to be of value, even then a selection of suitable patients is necessary. Considering that the neurogenic factor is the main cause of sustained vascular spasm, numerous tests have been devised to measure and eliminate this factor. There are a number of such tests, among them those that depend upon the response to Amytal, Pentothal, Etamon, and other substances. In spite of the apparent soundness of the reasoning which suggested these tests, experience has proved that such tests are often misleading. We have all been disappointed with the results obtained in patients with strongly positive tests who did not obtain the benefit expected from the sympathetic denervation. Conversely, we have all had patients in whom a poor result was expected after operation because of negative tests, and yet in whom a great reduction of blood pressure occurred. On this point opinion tends to be uniform; the tests proposed up to the present time are absolutely uncertain and cannot be relied upon in the selection of patients.

Objective tests do not furnish a sound basis for the selection of hypertensive patients suitable for surgery, in our opinion. The method we follow is a simpler one. It consists simply in recommending operation to those patients who need it, so long as there is no positive contraindication. This method requires only that one know which hypertensive patients are in need of surgical treatment and what conditions and circumstances positively contraindicate surgery. Numerous combinations of factors may be present and may make the clinical picture an apparently complex one. We believe that the problem of selection may be simplified by dividing the patients with essential hypertension into four groups according to the importance of their disturbance and the stage of their disease.

Group 1.—This group is made up of those patients with slight or moderate hypertension which has not produced vascular or visceral complications. Evidently these patients are not in need of the operation. Medical treatment only is indicated.

Group 2.—This group is composed of patients with severe hypertension, especially diastolic, who have not yet shown any important complications. Patients in this group have no vascular sclerosis or, at most, incipient sclerosis, their hearts are normal, their eye grounds fit into Type I or even II of Wagener and Keith's classification, and, finally, their renal function tests are normal. This group of patients is the one considered, in principle, as ideal for surgical treatment. Indeed, it is the group in which expectation of success is greatest and the risks slight. In practice, however, patients in this group very often do not accept

the recommended operation; moreover, the physician on his part does not feel justified in strongly urging a resort to surgery. When there is as yet no complication, it is not easy always to convince a patient to face an immediate risk in order to avoid a future danger. Surgical indication, at least in our experience, is somewhat illusory in this group of patients with uncomplicated hypertension.

Group 3.—This group includes patients who have severe hypertension and who show definite evidence of visceral complication, although these complications are not yet advanced. In the majority of patients there is present definite hypertensive heart disease with cardiac enlargement and even a gallop rhythm and an abnormal electrocardiogram. In some patients in this group, the evidences of cardiac strain may not be so marked, yet there may be evidence of encephalopathy (Grade 3 eye ground changes) or evidence of early renal sclerosis. In patients who fall into Group 3, although there is present easily recognizable structural damage, there does not yet exist functional insufficiency of an advanced nature.

Patients in this group have been generally considered as undesirable for surgery. Arteriosclerosis and structural visceral involvement which these patients show have been regarded as irreversible and as contraindications for operation. There is a mistake in this conception, at least in so far as it concerns those with cardiac complications. Limiting our consideration to these, we may say that, save for those in whom very special reasons exist, it is the patients in this group who most urgently need surgical intervention. Possibly brain and kidney damage is not likely to regress, but the same is not true of the heart. In cardiac damage, the most frequent complication, the physician may feel perfectly justified in insisting upon operation, and the patient, who is already confronted with the already existing ominous risk, may well accept the lesser risk of surgical treatment.

It is true that anatomical damage is already present in the heart, but when this is of slight degree, it is in a way reversible when the hypertension is corrected. On the other hand, since cardiac damage is not yet severe, it does not add to the risk of the operation. The onset of heart damage is a call for help. Since medical treatment is incapable of suppressing the cause, surgical intervention is the only means available for giving help to the strained heart.

Opinions already expressed by others give some support to the recommendations that are being made. White[10] states categorically that hypertensive heart disease "is more an indication of the necessity of operation than a contraindication as was previously thought." Allen[1] is less categoric and he limits his statement by saying that "albuminuria and moderate heart enlargement do not constitute a contraindication." Peet and Isberg[7] maintain that "heart enlargement and an abnormal electrocardiogram are not a contraindication for operation."

To support the opinion that patients with elevated blood pressure and with definite cardiac change should be operated upon before they develop functional cardiac insufficiency, we have carefully studied and followed a series of patients. The results confirm this opinion. Very recently, Isberg and Peet[5] presented a large survey of 275 patients with hypertensive heart disease, 60 per cent of whom

are living five to thirteen years after operation; in this series intervention was more efficacious in patients with less advanced disease.

Group 4.—This group includes patients with more advanced hypertensive disease, who have severe visceral complications consisting of heart failure, renal insufficiency, or severe encephalopathy.

Opinions have been unanimous for a long time that patients who belong in this group should not be operated upon. Summarizing the experience at the Mayo Clinic, Allen maintains that it is useless to operate upon a patient who has had heart failure, auricular fibrillation, angina pectoris, severe renal insufficiency, or high grade hypertensive encephalopathy. Peet and Isberg[7] agree with this view and state that "in these cases, lasting benefit is seldom attained." Padilla and Cossio[6] report only temporary improvement in five patients with heart failure who were operated upon, and for this reason they are not in favor of surgical treatment in this type of patient.

Yet, even in this group of patients, it seems that such a positive decision should be modified, at least for those patients in whom heart failure constitutes a major disability. In the same way that the patients in the previous group, who were formerly rejected, are now known to be amenable to surgery, so the patients in this group are subject to benefit from operation.

Considering the problem fundamentally in terms of the heart and not of cerebral and renal complications, since the latter lesions do not have the same tendency to regression that exist in cardiac lesions, it is conceivable that the mechanical factor of overwork and strain plays a decisive role in producing and later maintaining heart failure. It is true that in the genesis of heart failure there is another factor besides the mechanical one: that of coronary sclerosis with defective myocardial blood supply. Nevertheless, without the excessive work originated by the high pressures, there would not be failure and the damage to the coronary arteries would be stopped or at least delayed.

No form of therapy for the heart failure of the hypertensive patient is logical unless it lowers the blood pressure. Rest and digitalis therapy, which have constituted our only means of treating these patients up to this time, have only temporary efficacy. As long as hypertension, that factor which fatigues and strains the heart, continues to act, relapses are inevitable, and with each relapse the damage to the heart becomes more severe.

Up to the present, only White[10] has supported the view that a certain degree of heart failure, if not advanced, is amenable to surgical treatment. Isberg and Peet,[5] on their part, have recently modified somewhat their earlier sceptical attitude: In sixteen operated patients with heart failure they report a survival of over five years in five patients. In view of this fact, they maintain that resort to surgical intervention "should not be denied once the patient is properly digitalized."

We, on our part, have been forced to go farther and to try surgical intervention in patients with desperate grades of hypertension who have developed severe heart failure, even when the failure is intractable and resistant to digitalis treatment. Our experience offers legitimate hope. We shall summarize the results in our first case, which justifies this heterodox opinion.

In April, 1945, one of us (I. C.) recommended Smithwick's operation to a 50-year-old business man, a very nervous individual with severe hypertension who had been under treatment for two years. In the beginning his blood pressure was around 250/150 and could not be lowered by the usual medical treatment, including thiocyanate. Later, heart enlargement developed, and then heart failure with presystolic gallop rhythm and visceral congestion appeared, both rapidly subsiding with rest and ouabain. Still later, repeated relapses occurred. With these relapses there were alarming paroxysms of nocturnal dyspnea and diastolic hypertension up to 160 mm. of mercury. Medical treatment gradually became ineffective, digitalis and ouabain lost their efficacy, and the patient spent night after night in tormenting asphyxia.

When the situation became intolerable and medical treatment had nothing to offer, the patient accepted operation, knowing the great risk involved. Medical treatment was redoubled until the patient was brought into the best possible condition. Dr. Clemente Robles performed the operation at the Institute in April, 1945.

After a tormented postoperative period, evident improvement followed. Hypertension was reduced from 220/160 to 190/110 in the recumbent position and 170/110 in the standing position; heart failure soon subsided and disappeared in the course of two months; the electrocardiogram was favorably modified though it did not become normal; the eye grounds did not change. Against medical advice, the patient returned to a normal, active business life four months after operation. At the present time, three years after operation, he is traveling through Europe in very good condition. The patient apparently presented a definite contraindication to surgery. The results proved that there are no absolute contraindications.

As a result of the experience gained from this patient, we have subjected to operation ten additional patients in the Institute of Cardiology, all of whom had hypertensive heart disease and heart failure of variable degrees. The results are summarized in Table I.

In the total of eleven patients there has only been one death which can be attributed directly to surgery; and another fatality should be judged with certain reservation. Death in the first patient was due to a cerebral hemorrhage eleven days after operation. Death in the second patient occurred the day after operation and was due to occlusion of the aqueduct of Sylvius by a fibrinous thrombus: the existence of an old meningitis had been overlooked. A third patient died ten months after operation; death was due to the natural progress of his disease and to the development of uremia. The other eight patients were cured of their heart failure and they have not relapsed after follow-up periods ranging from one to three years. Almost every patient has resumed a normal life and the blood pressure is only slightly elevated, if not normal.

This small group is impressive if one considers that it is made up of patients with the most severe grade of hypertensive heart disease with heart failure: a type of patient who was previously rejected from surgery. It is impressive also because of the unexpected proportion of successes: 75 per cent.

TABLE I. RESULTS OF SYMPATHECTOMY IN ELEVEN PATIENTS WITH HYPERTENSIVE HEART DISEASE AND HEART FAILURE

NO.	AGE (YEARS)	BLOOD PRESSURE BEFORE OPERATION	BLOOD PRESSURE AFTER OPERATION		HEART ENLARGEMENT	HEART FAILURE	RECOVERY FROM HEART FAILURE	FOLLOW-UP PERIOD (YEARS)
			RECUMBENT	STANDING				
1	50	240/140	180/120	160/110	++	++++	Complete recovery	3
2	35	185/155	170/120	130/90	+++	+++	Complete recovery	2½
3	41	185/115	170/100	140/80	++	++	Complete recovery	2
4	50	250/130	180/110	150/100	+	++	Improvement	2
5	61	180/110	160/100		+	+	Considerable improvement	2
6	46	210/110	220/110	170/100	++	+++	Slight improvement	2
7	38	200/130	170/110	170/100	+	++	Considerable improvement	1½
8	29	230/150	170/80	160/80	++	+	Considerable improvement	1½
9	36	260/160	200/120	200/120	+++	++++	Death 10 months after operation (uremia)	
10	57	200/140	——	——	+++	+++	Death 11 days after operation (cerebral hemorrhage)	
11	51	210/140	140/110	——	++	++	Death the day following operation (occlusion aqueduct of Sylvius)	

The barrier which formerly barred from surgery patients classified as Group 3, hypertensive patients with secondary heart disease, has been pushed back gradually in the last six years. Now only patients who fall into Group 4, that is, hypertensive patients with heart failure, are deprived of sympathetic surgery.

On the basis of the results presented today, it is seen that this limitation is not always justified. We do not intend, of course, to advocate surgical treatment for all patients with hypertensive heart disease which has reached the final stage of heart failure, but there are times when it is better to disregard the apparent contraindications. Since there is no effective medical treatment for lowering the blood pressure, surgery is the only form of treatment capable of giving relief to the heart when rest and digitalis have lost their effectiveness. In support of this view, we offer this group of hypertensive patients in the final stage of heart failure, at times of advanced nature, who have been treated surgically with success.

We admit that the operative indication which we have discussed is simply an indication in principle. Our recommendation of surgery is made broadly. A number of added factors must be considered and their presence may clearly contraindicate surgery. These factors are chiefly advanced damage to the coronary arteries and advanced myocardial degeneration. Only such considerations as the careful evaluation of these factors, of the existing visceral complications, and of the resistance of the patient to operation will permit the physician to decide in each case whether surgical intervention is indicated or not. In advanced cases of hypertensive heart disease in which the heart is greatly enlarged, the coronary arteries are severely damaged, and heart failure is long standing, operation is clearly contraindicated. In moderate cases, on the contrary, it is probable that the treatment will have to be both medical and surgical in the future.

SUMMARY AND CONCLUSIONS

In the surgical treatment of arterial hypertension by means of sympathetic denervation, it has been considered up to the present time that hypertensive heart disease and especially heart failure were formal contraindication to operative procedure. Unfortunately, patients with these handicaps are precisely the ones who most urgently need lowering of their blood pressure.

When medical treatment has failed we have been forced at the Instituto Nacional de Cardiologia to operate upon a number of hypertensive cardiac patients, all of whom were in heart failure which in some was of extreme degree.

Of the eleven patients operated upon, one died from cerebral hemorrhage eleven days after operation; another succumbed the day after the operation from occlusion of the aqueduct of Sylvius, the result of an overlooked old meningitis; a third patient died ten months after operation in uremia.

The other eight patients improved ostensibly and for a long time; they are still alive after one and one-half to three years and have shown no evidence of heart failure since operation. Some of them have resumed normal life.

We feel that instead of being a contraindication, hypertensive heart disease is fundamentally a formal indication for surgical treatment as the only means of staying myocardial damage.

We believe furthermore that heart failure, when it is not accompanied by very advanced lesions, may sometimes be corrected through the operative procedure, even in protracted cases where digitalis and ouabain have failed.

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THE CORONARY VASODILATOR ACTION OF KHELLIN

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OUR interest in Ammi Visnaga and its active principle, "khellin," arose as a result of an accidental observation. For the last three years a member of our laboratory staff has been suffering from definite symptoms of coronary insufficiency. Anginal attacks were frequent; they occurred not only after exertion but also spontaneously, especially after meals, and sometimes even at night. In addition to his coronary complaint, the man became a victim of renal colic of such severity that he had to stop his work. X-ray examination revealed the presence of three calculi in the left ureter. After taking various remedies without much benefit, he was advised to try a tincture of Ammi Visnaga. This apparently was of some help; at any rate, on the seventh day he passed some sand and a calculus. At the time we were not aware of his condition and our attention was drawn to him only after his return to work. The man, who usually behaved like a semiinvalid, appeared stronger and more vigorous; he moved faster, lost his apprehensive and frightened look, and could climb the staircase without the usual attacks. He said that he was free from attacks also during the rest of the day. He attributed his improvement to the passage of the calculus, which, however, proved to be wrong since a few days later his general condition became as bad as before. On investigation we found that during the period of colic the man consumed up to 20 c.c. of tincture of Ammi Visnaga per day. On the off chance that visnaga was the cause of his temporary improvement, we persuaded him to repeat the treatment. The relief which followed was so unmistakable that he has continued to take the drug for over two years.

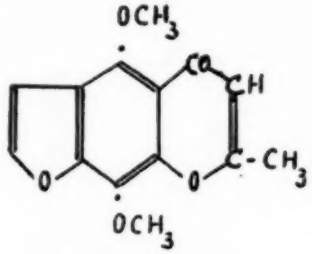
As a result of this observation we decided to investigate the action of Ammi Visnaga on the cardiovascular system with special reference to the coronary blood flow and the heart muscle.

The considerable amount of experimental and clinical observation which has at present accumulated gives a sufficiently sound foundation for a comprehensive review of the therapeutic value of the various crystalline principles which have been extracted from the fruit of Ammi Visnaga. This plant, known in Arabic as "Khella," grows wild in the Eastern Mediterranean countries. The local population has been using decoctions of its seeds as an antispasmodic since ancient times.

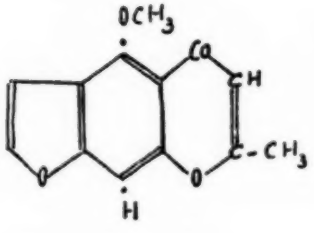
From the Physiological Laboratory and Fouad I University Hospital, Kasr-El-Aini, Cairo, Egypt. Presented before the Third Inter-American Cardiological Congress, Chicago, Ill., June 13-17, 1948. Khellin was supplied by the Alpha Laboratories, Cairo, in the form of *Ammicardine*.

So far, three distinct crystalline substances have been extracted and isolated from the seeds in a pure form. The three substances, the molecular and structural formulas of which have been determined, are as follows:

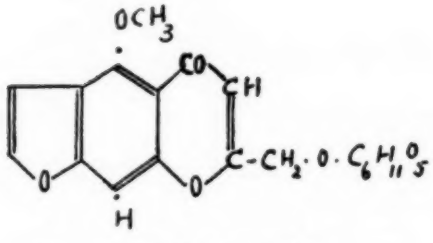
1. Khellin: This substance was first prepared in an impure form by Mustapha[1] in 1879, who also suggested the name, and again by Malosse[2] in 1881. Fantl and Salem[3] in 1930 isolated pure khellin, determined its composition, and suggested a structural formula which was somewhat modified subsequently by Spaeth and Gruber[4] in 1938. Chemically, khellin is a dimethoxy-methyl-furano chromone (Fig. 1).



I Khellin.



II Visnagin



III Khellol-glucoside.

Fig. 1.—The structural formulae of the substances the biological action of which is described in this communication.

2. Visnagin: This substance was first isolated by Spaeth and Gruber[5] in 1941, who found it to be a monomethoxy-methyl-furano chromone (Fig. 1). Visnagin is found in the seeds in negligible amounts.

3. Khellol-glucoside: This substance was first isolated and named by Fantl and Salem[3] in 1930. The structural formula of this substance was determined by Spaeth and Gruber[6] in 1941, according to whom it is an oxyglucoside of visnagin (Fig. 1). Khellin and the glucoside are found in the dried seeds in approximately equal amounts.

In 1931 the pharmacognosical features of the two main crystalline substances were studied by Fahmy[7,8] and in 1934 the decoction and the tincture of Ammi Visnaga were included in the Egyptian pharmacopeia. Samaan in 1932 investigated the biologic action of khellin[9] and of the glucoside[10] which he called, respectively, "visamin" and "khellinin." We prefer to use the names originally given to these substances by the workers who first isolated and analyzed them. Furthermore, the original nomenclature has been widely used in the German and English literature. The name "visamin" seems to us unsuitable also because it might imply the presence of an amino group, which is not the case.

According to Samaan,[9] khellin causes a relaxation of all the visceral smooth muscles, while the glucoside has no special action. No further investigation of these substances seems to have been made until Anrep, Barsoum, Kenawy, and Misrahy[11] demonstrated that khellin causes a conspicuous dilatation of the coronary blood vessels. The minimal effective concentration of the drug causing definite coronary vasodilation in the heart-lung preparation in dogs was found to be of the order of 10^{-6} which is considerably smaller than for aminophyllin and other xanthine derivatives. With concentrations of 10^{-5} the coronary sinus outflow increases up to three times the initial volume. The action of khellin, although very considerable, is less than that of amyl nitrite, but it has the advantage of being much more prolonged. Gradual administration of khellin up to concentrations of 10^{-4} has no undesirable effect on the heart muscle, on respiration, or on the general blood pressure. Rapid intravenous injections of large doses of khellin cause a temporary drop of the blood pressure; but no such effect was ever observed when the drug was injected slowly into the veins or administered intramuscularly. It was further found by Anrep, Barsoum, and Kenawy[12,13] and later by Bagoury[14] that in somewhat larger doses khellin causes coronary dilatation also in the isolated perfused rabbit heart and that it relaxes the bronchial musculature of the guinea pig even after an artificially induced spasm caused by the administration of histamine. Administration of concentrated solutions of khellin, as happens when the drug is injected into the cannula perfusing the isolated heart, weakens the heart muscle. The drug should be administered in very dilute solutions. No such weakening was observed in the blood-perfused heart-lung preparation. Fig. 2 is a graphic representation of the effect of khellin on the coronary sinus outflow in the heart-lung preparation.

Similar results were also obtained in experiments made on the whole animal after its blood was rendered uncoagulable with a mixture of heparin and chlorazol fast pink.

The observation of Samaan[9] that khellin causes a relaxation of the intestinal musculature was confirmed on the isolated intestine and in the whole animal. Methods were devised for the biological assay of khellin in the blood

and the tissues, and the colorimetric method first suggested for this purpose by Fahmy was improved by Anrep, Kenawy, Barsoum, and Fahmy.[15] The improvements in the assay of khellin allowed us to study the rate of its absorption and to determine its concentration in the blood and tissue at different periods of time after administration of the drug.

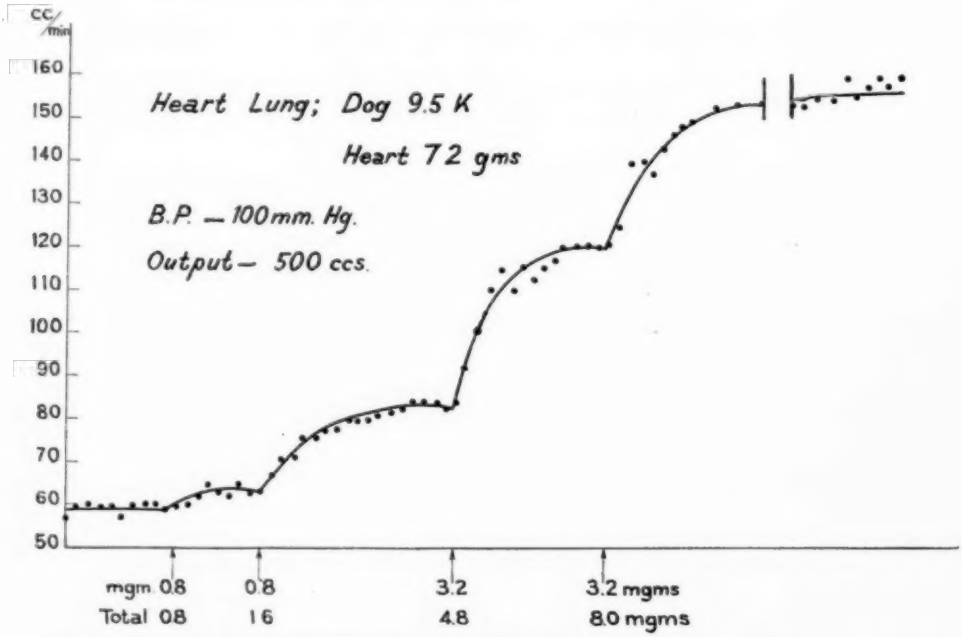


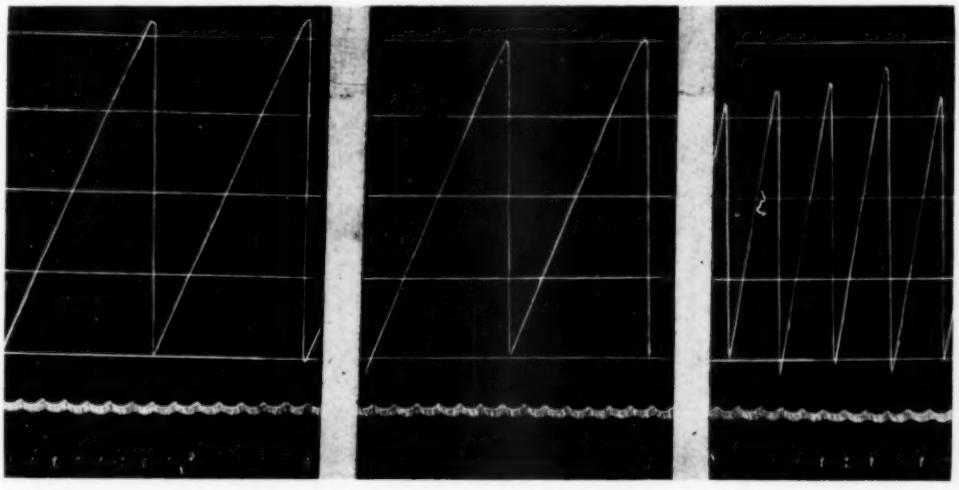
Fig. 2.—The coronary vasodilator action of khellin as measured by the sinus outflow of blood in the heart-lung preparation. The total amount of blood in the circulation was about 900 cubic centimeters. The gap in the curve corresponds to an interval of twenty minutes. The drug was administered into the venous reservoir of the apparatus.

Intramuscularly administered, khellin is rapidly absorbed[16] into the circulating blood, reaching a maximal concentration in five to seven minutes. It is also rapidly absorbed from the stomach and from the small and the large intestines, the maximal concentration in the blood being reached in ten to fifteen minutes. After absorption, khellin becomes approximately uniformly distributed in all the tissues and organs of the body, a fact which has to be taken into consideration in the calculation of the effective dose to be administered. The destruction and excretion of khellin after it has been absorbed is slow. After an interval of twenty-four hours its concentration in the tissues is approximately halved and traces of the drug can be found in the blood and tissues as late as four days after its administration. The concentration of the drug in the blood does not diminish more rapidly than in the tissues, which indicates that the latter serve to store the active principle. This also explains the prolonged action of the drug.

Because of the prolonged retention of khellin in the body, repeated administrations of the drug have a cumulative effect. The saturation of the organism

with the drug gradually increases. For example, thirty minutes after the first intramuscular injection of 200 mg. of khellin in man, its concentration in the blood was 4 to 6 μg. per cubic centimeter; after five further similar injections, one per day, the concentration of khellin in the blood rose to 15 μg. per cubic centimeter. Five days after the last injection the blood of the subjects still contained about 2.5 μg. per cubic centimeter.

Experiments with the khellol-glucoside[15] gave completely negative results. This substance causes no relaxation of the smooth muscles and no coronary vasodilation (see Fig. 3). Furthermore, it was shown that the glucoside is not changed in the body into the active khellin and that, in fact, the glucoside is not even absorbed from the gastrointestinal tract. We consider, therefore, that the glucoside presents no therapeutic interest.



A. *B.* *C.*

Fig. 3.—Heart-lung preparation. Top tracing is the coronary blood flow as measured by a volume recorder. The horizontal lines are graduations of 10 c.c. each.

The middle tracing is the blood pressure in mm. Hg and the bottom tracing is time in ten-second intervals. Mean systemic arterial blood pressure was 120 mm. Hg.

***A*, Normal coronary blood flow (55 c.c. per minute).**

***B*, Coronary blood flow after injection of 100 mg. of the glucoside (55 c.c. per minute).**

***C*, Coronary blood flow after injection of 10 mg. of khellin (145 c.c. per minute).**

With regard to the third crystalline principle of Ammi Visnaga, namely, visnagin, its biologic action is similar to that of khellin except that it is about 30 per cent weaker. It occurs in the seeds in such small quantities that it presents no special interest. It is also rather difficult to separate visnagin from khellin since both are soluble in the same solvents, which is not the case with the glucoside which, therefore, can be removed easily from the extracts.

The action of khellin on the systemic blood vessels and, therefore, on systemic blood pressure can be completely discounted when therapeutic doses are used. The concentration of the drug must exceed all reasonable limits to cause a

relaxation of the systemic blood vessels. In this respect one can consider the action of khellin on the coronary blood vessels, as nearly as possible, a selective one.

The kidney function is not impaired by prolonged administration of the drug. The old view that khellin causes a diuresis could, however, not be confirmed by Salama[17] in 1946.

As stated before, the value of the decoctions of Ammi Visnaga as an antispasmodic has been realized since ancient times; it has not, however, been used until recently except in cases of ureteral spasm to help the passage of ureteral calculi. The experimental findings summarized here open at least three new lines of investigation, namely, the use of khellin in the treatment of the anginal syndrome, the treatment of bronchospasm, and the treatment of gastrointestinal spasm and also the spasm accompanying gastroduodenal ulceration. The results of our observations upon bronchial asthma and the gastrointestinal tract at present are in preparation for the press; the rest of this communication is devoted to the treatment of the anginal syndrome.

COMPARISON BETWEEN KHELLIN AND AMINOPHYLLIN

A series of comparative observations were made upon the action of khellin and that of aminophyllin on the coronary circulation and on smooth muscle. The action of khellin on the bronchi of the guinea pig was found to be about four times stronger than that of aminophyllin, while when tested on the rectal caecum of the fowl,[18] khellin was twelve times more effective than aminophyllin.

The comparison of the coronary vasodilator action of the two drugs was made on the heart-lung preparation and on the isolated rabbit heart. For obvious reasons, the testing of the two drugs could not be made on the same heart-lung preparation. Therefore, the action was studied on two separate preparations, the separate studies being done as nearly as possible under the same experimental conditions. The type and weight of the dogs used for the two preparations was the same; the arterial blood pressure, the temperature, and the cardiac output, as well as the total amount of blood in the circulation, were kept the same and the two hearts usually did not differ in weight by more than 5 grams. In spite of the limitations imposed by such a method of comparison, the difference in the action of khellin and of aminophyllin was unmistakable. The following comparative experiment serves as an example.

In the first heart-lung preparation the coronary sinus outflow increased after administration of 10 mg. of khellin from 41 c.c. per minute to 120 c.c. per minute. In the second preparation the outflow was 36 c.c. per minute before and 39 to 40 c.c. per minute after administration of 20 mg. of aminophyllin; after a second dose of 20 mg. the outflow increased to 84 c.c., and after a third similar dose, to 125 c.c. per minute.

On the basis of other similar experiments, as well as experiments in which the blood flow was measured in the left coronary artery, we conclude that khellin is at least four times more effective as a coronary dilator than aminophyllin.

Observations on the isolated rabbit heart present the advantage that the two drugs can be administered in succession in the same heart. It must be

remembered, however, that the rabbit heart is less sensitive than the blood-perfused heart in the heart-lung preparation. The following experiment serves as an illustration of the results obtained by this method.

The rabbit heart was perfused with oxygenated Ringer-Lock solution through a three-way cannula which could be alternately connected to a reservoir containing a normal solution, to another reservoir containing khellin, or to a third reservoir containing aminophyllin. The perfusion pressure was kept at 120 mm. Hg and the temperature at 38° centigrade. The results are shown in Table I.

TABLE I. COMPARISON OF EFFECTS OF KHELLIN AND AMINOPHYLLIN UPON CORONARY BLOOD FLOW IN THE ISOLATED PERFUSED RABBIT HEART

PERFUSING SOLUTION	CORONARY OUTFLOW IN C.C. PER MINUTE, MEASURED AT MINUTE INTERVALS
Ringer-Lock	7.6, 7.4, 7.5, 7.6, 7.4
R-L solution plus 10 μg./c.c. of khellin	7.6, 8.5, 10.2, 13.4, 14.0, 14.2, 14.1, 14.2
Ringer-Lock	14.0, 13.2, 12.0, 10.6, 8.3, 7.7, 7.2, 6.9, 7.3
R-L solution plus 30 μg./c.c. aminophyllin	7.3, 7.7, 8.7, 9.1, 8.8, 8.6, 8.7, 9.0, 8.8
R-L solution plus 40 μg./c.c. aminophyllin	9.5, 10.2, 11.1, 13.6, 12.9, 13.3, 13.6
After perfusion with normal Ringer-Lock solution the coronary outflow returned to an average of 6.0 c.c. per minute when khellin was administered for a second time.	
R-L solution plus 10 μg./c.c. khellin	6.0, 6.9, 7.9, 10.2, 11.7, 12.1, 13.2, 13.0

The experiments upon the isolated heart thus confirm the results obtained on the heart-lung preparation. The action of khellin is thus about four times stronger than that of aminophyllin.

TREATMENT OF CORONARY ARTERY DISEASE

Khellin was clinically tried on 300 patients suffering from coronary artery disease. The cases fall into two groups: (1) 250 patients with angina of effort or decubitus; (2) 50 patients with coronary thrombosis, with or without anginal attacks during the period of absolute recumbency.

Khellin was used either as a continuous treatment to prevent or diminish the number of attacks or occasionally for the relief of the actual attacks. The subjective effects of the drug were recorded in every case. Most of our patients were more or less stable and knew the amount of exercise which would evoke an attack. Most of them had been treated previously with other coronary vasodilator drugs such as aminophyllin and theophyllin. Objective tests were carried out on some of the patients by registration of the electrocardiographic changes caused by graded exercise before and after administration of khellin. Controlled exercise tolerance tests were made whenever the condition of the patient allowed. Patients giving a history of a recent coronary thrombosis or showing any signs of myocardial failure were exempted from these tests. To eliminate any possible interference of a psychic element in the action of the new drug, placebos were

administered either in the form of injections or tablets containing no khellin, or, without the patient's being informed, the dose of khellin was suddenly reduced. No other drugs were given during the treatment except, when necessary, an occasional trinitrin tablet to some of the patients.

Method of Administration.—Khellin was administered in the following forms: (a) As a purified liquid extract containing 50 mg. of the active principle per cubic centimeter. The dose is 1.0 to 2.0 c.c. diluted with water. This preparation has a bitter taste and should be taken preferably with meals. (b) As tablets, each containing 50 mg. of khellin; one to two tablets are to be taken after meals. (c) As intramuscular injections in a strength of 50 mg. per cubic centimeter; 2 c.c. are injected once or twice daily and during anginal attacks. The injection causes a slight local pain which lasts a few seconds.

In most of our cases, the tablets or liquid extract were used, but in severe cases a combined treatment using injections as well as oral therapy was resorted to. The minimal effective daily dosage was calculated as 2.0 mg. per kilogram of body weight.

Results in Patients With Angina Pectoris.—

Our preliminary clinical trials of khellin were published in 1945 and 1946.[19,20] The results were encouraging and justified further investigation. Reports confirming our results have been published by Ayad.[21] The 250 patients comprising the group with angina pectoris were subjected to khellin treatment. The cases were divided into three classes according to the severity of the condition. Eighty patients were classed as being mild cases, 115 as moderate, and fifty-five as severe. The group comprised 225 men and twenty-five women and their ages varied between 35 and 76 years. The duration of the anginal symptoms was between three and fifteen years in 168 cases, between one and three years in fifty-two cases, and less than one year in thirty cases. Hypertension was present in eighty-four cases and diabetes mellitus in eighteen. The Wassermann reaction was negative in all except three patients. The electrocardiogram was abnormal in 102 cases and the heart was hypertrophied in fifty-nine cases. In eighteen cases the anginal symptoms appeared after an attack of coronary thrombosis.

Response to Treatment: The response to khellin was arbitrarily classed as good, moderate, or negative; good when the anginal attacks ceased altogether or became very infrequent and mild, moderate when they diminished in frequency and severity, and negative when no favorable change occurred. On this basis the results are summarized in Table II. The duration of observation and treatment varied from three months to two years, being eight months or longer in two-thirds of the cases, excluding those classed as failures.

Continuous Treatment: Oral treatment was given to most patients, except when a response was delayed or the case was severe. Under these conditions combined oral and parenteral treatment was used in order to produce a high level of khellin in the blood. Response to treatment occurred after three to five days in mild and moderate cases and after seven to ten days in severe cases. Optimal

improvement is always expected after two weeks' treatment. As previously stated, the drug is cumulative and is slowly excreted from the body. When improvement is obtained, a maintenance dose of 50 to 100 mg. or even more, according to the severity of the case, can be given for many months or even years without any untoward effects.

TABLE II. THE RESPONSE TO KHELLIN OF 250 PATIENTS WITH ANGINA PECTORIS

GRADE OF ANGINAL PAIN	RESPONSE TO TREATMENT		
	GOOD	MODERATE	NEGATIVE
Mild	68	12	—
Moderate	56	55	4
Severe	16	18	21
Total	140	85	25
Percentage	56	34	10

It can be seen from Table II that 56 per cent of the patients showed good improvement, 34 per cent showed moderate improvement, and 10 per cent failed to respond. If the drug was discontinued for a few days or replaced by a placebo, the attacks reappeared, sometimes in a milder form. No habituation to the drug was ever noticed during our investigations.

Treatment of Individual Attacks: The liquid extract was given to patients during the attacks, and relief was obtained in more than 70 per cent of the cases. In the case of more prolonged attacks, intramuscular injections of 100 mg. brought relief in a few minutes. On the whole, the relief obtained was slower than after trinitrin tablets.

Objective Tests: Some of the patients were subjected to standardized exercise tolerance tests by stepping on a chair 40 cm. high at the rate of thirty times per minute. Electrocardiograms were taken before and after the exercise. The exercise was continued until the patient felt definite precordial pain. A few hours later or on the next day, the same exercise was performed thirty minutes after an intramuscular injection of 100 mg. of khellin and the electrocardiogram was again recorded. The RS-T depression and T-wave inversion occurring after the exercise test were prevented by khellin administration. In some cases the same test was repeated after one or two weeks' continuous treatment. In all patients tested, the exercise tolerance increased after khellin. Fig. 4 is an example illustrating the effect of khellin on the electrocardiogram taken after exertion before and after the drug.

Electrocardiographic tracings were also taken on dogs weighing about 12 kilograms in order to investigate whether massive doses of the drug produce electrocardiographic change. Two hundred fifty mg. injected intramuscularly or intravenously produced no electrocardiographic changes.

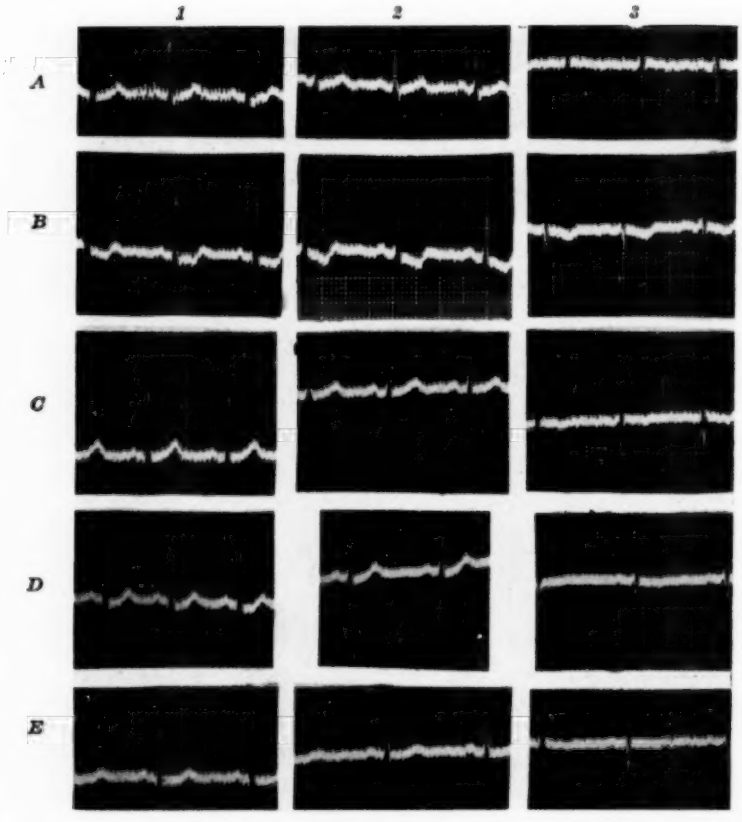


Fig. 4.—*A*, Electrocardiogram before and, *B*, after exertion, showing marked RS-T depression and inversion of T wave.

C, Electrocardiogram before khellin injection.

D, Electrocardiogram immediately after injection of 100 mg. khellin.

E, Electrocardiogram taken after exertion thirty minutes after khellin injection. Note absence of RS-T depression or inversion of T wave.

Side Effects: Some of our patients complained of a sensation of warmth. A few patients complained of mild dyspeptic symptoms after oral administration. Insomnia was also complained of by a few patients. Neither meteorism nor abdominal distension was observed in our series of patients.

The coagulation and bleeding times were estimated in almost all patients and found to be unaffected. The blood pressure, pulse rate, and respiration were unaffected by doses of khellin up to 200 milligrams.

Results in Patients With Coronary Thrombosis.—

Fifty patients with acute coronary thrombosis were subjected to khellin therapy. Twelve patients died during the first or second week of the treatment and thirty-eight patients recovered. In some of these patients the illness was a serious one from the start, but patients with equally serious involvement recovered after khellin treatment. It is very difficult to attribute any improvement to

one or another cause and therefore it is too early to reach definite conclusions. Comparing one group of fifty patients with coronary thrombosis who received khellin with another group of fifty patients who received other coronary vasodilator drugs, there was not much difference in the mortality rate. In the control group, fourteen patients died.

Khellin, together with morphia, was given safely in single doses of 100 mg. and continued in this dosage daily for a period varying from six weeks to three months. The drug controlled and relieved the anginal attacks which followed coronary thrombosis during the period of rest in bed as well as after recovery in twenty-one patients who happened to suffer from such attacks.

The main object of administering khellin to patients with coronary thrombosis was to provide the heart with a coronary vasodilator agent which does not lower the blood pressure or affect the heart muscle. It was also hoped by this therapy to relieve any associated coronary spasm and improve the collateral circulation, and in this way to diminish the area of the cardiac infarct.

Three patients with coronary thrombosis also suffered from auricular fibrillation; all three patients tolerated the drug fairly well and made a good recovery. The drug also appeared to relieve attacks of cardiac asthma occurring in two patients of our series.

COMMENT

Experimental as well as clinical observations show that Ammi Visnaga and its active principle, khellin, can be used as a coronary dilator in the treatment of deficient coronary circulation. As a result of its administration in a series of patients, the number of anginal attacks became less and the cardiovascular tolerance increased. No habituation to the drug seemed to occur. Even after the drug was used for two years, it was still effective. No toxic effects were encountered during its trial for such periods. The drug seems to be safe to administer as well as of value in relieving the coronary spasm occurring during coronary thrombosis. Administered during attacks of angina, it causes relief.

Khellin possesses definite advantages over other known coronary vasodilators. Compared with aminophyllin, for example, the action of khellin is more prolonged; dose for dose, khellin is more potent than aminophyllin. Experimental evidence has shown that the effect of khellin on the coronary blood vessels is about four times stronger than that of aminophyllin. Aminophyllin stimulates the myocardium to increased vigor of contraction. This is accompanied by increased cardiac output and increased work of the heart. Some authors suggest that the increase of the coronary blood flow produced by theophyllin in the experimental animal follows rather than precedes the myocardial stimulation. Khellin does not lower the blood pressure in man, while aminophyllin may affect the blood pressure; this varies according to its method of administration. Khellin does not affect the blood coagulability as aminophyllin is said to do.

SUMMARY

The experimental observations show that khellin is a potent coronary vasodilator; the minimal active concentration of the drug is 10^{-6}. Khellin has a very prolonged action and remains in the circulation for many hours. Its action in dilating the coronary arteries was compared with the similar action of aminophyllin; khellin was found to be at least four times stronger than aminophyllin.

Khellin can be used continuously in the treatment of angina pectoris and also for the relief of individual attacks of pain. It can be administered orally in doses of 50 to 100 mg. three times per day, or as an intramuscular injection in doses of 100 to 200 milligrams. The drug produces a few side effects but is not toxic even after prolonged administration. It does not affect the bleeding or coagulation time.

Altogether 250 patients with angina pectoris were treated with khellin with distinct improvement in 140 cases, with moderate improvement in eighty-five cases, and with no effect in twenty-five cases. In many patients clinical improvement was confirmed electrocardiographically. The drug was used also in fifty patients with recent coronary thrombosis with the object of improving the collateral circulation and relieving any associated anginal symptoms. The latter, at least, seemed to have been accomplished.

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FURTHER STUDIES OF THE CIRCULATION WITH RADIOACTIVE ERYTHROCYTES

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NEW possibilities of investigating the normal and pathological physiology of the human circulation have been opened by De Hevesy's method of labelling human erythrocytes with radioactive phosphate. We have used this method since 1942 to elucidate certain physiological and pathological problems, and have published several papers dealing with these problems. The circulating corpuscular volume has been determined with red cells labelled with radioactive phosphate.

General Method.—In general, the following method has been used: About 8.0 c.c. of blood, taken from an arm vein of the patient, is put into a paraffinized glass flask containing a small amount of heparin to prevent blood clotting, together with a minimal amount of radioactive sodium phosphate. The labelling activity is about 0.05 millicurie. The glass flask is shaken in a special water bath at 37°C. for two hours. By that time the blood corpuscles and the plasma are about equally labelled. About one-half of the 8.0 c.c. of labelled blood is reinjected into the patient and thereafter blood samples are drawn at fixed times after the injection. The activity of the injected samples, and also of the drawn samples, is then measured with a Geiger counter. The plasma and cells are treated separately in each sample. The activity has been expressed as "specific activity," that is, the impulses per gram of plasma or corpuscles per minute. In each experiment about 0.05 millicurie of activity has been injected into the patient. In general, in order to measure the circulatory corpuscular volume and changes in the circulation according to the mixing conditions, we have injected both labelled corpuscles and plasma, that is, the whole labelled blood. In nearly all of our publications we have paid especial attention to the mixing phenomenon in the human body and made rather comprehensive investigations on this extremely interesting question. The earliest part of the mixing curve (or dilution curve) has been achieved by collecting blood samples successively without interruption from the arterial blood practically immediately after the labelled blood has been injected intravenously into the patient.

In our routine determinations of the circulatory blood corpuscular volume we have not taken arterial but venous blood samples and measured the activity

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Presented before the Third Inter-American Cardiological Congress, Chicago, Ill., June 13-17, 1948.

of both corpuscles and plasma in them. With this technique we obtain the results of the specific activity of both plasma and corpuscles according to Fig. 1. We have found rather constantly, as is seen in Fig. 1, that the activity of the plasma decreases very rapidly from the sixth minute after the injection, with the result that there are minimal quantities left in the plasma one to twenty-five hours after the injection. On the other hand, the activity of the red cells remains practically constant up to one hour after the injection and then loses its activity rather slowly, so that six hours after the injection about 10 per cent is lost. The fact that the red cells retain their activity at a rather constant level for at least one hour after the injection makes this method a very suitable one for studying circulatory pnenomena. As a result of this it has been possible to study the changes in the circulatory corpuscular volume in cardiac decompensation (Hedlund) and the influence of the so-called depôt function following muscular exercise and the injection of adrenalin (Nylin). It has also been possible to measure the blood volume of one lung during pulmonectomy, of the lower part of the legs, and the change in the circulatory corpuscular volume after ligation of a patent

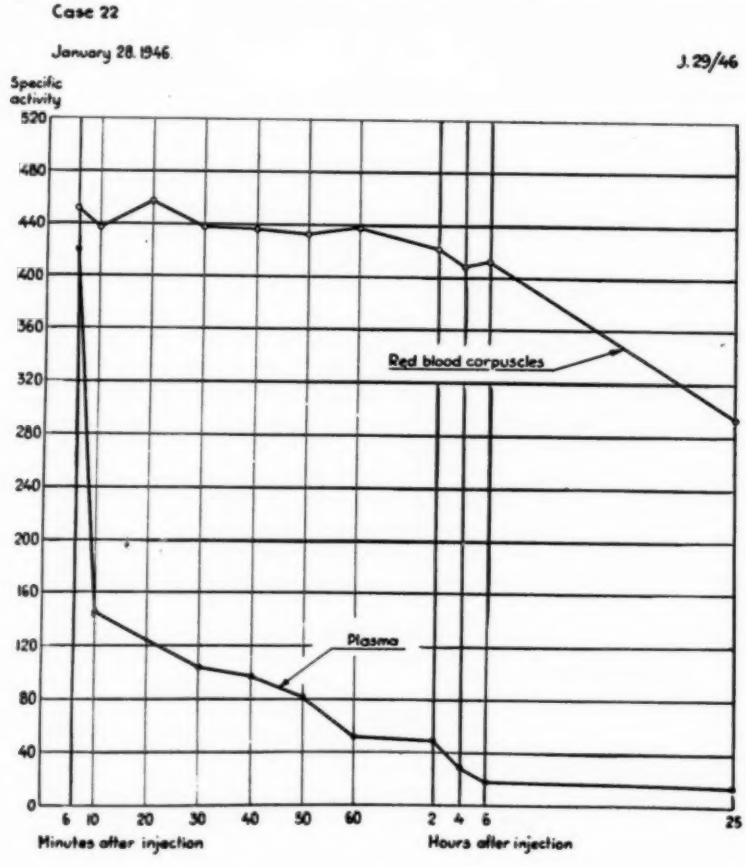

Fig. 1.—Specific activity of red blood corpuscles and plasma during twenty-four hours after intravenous injection of tagged erythrocytes and plasma.

ductus arteriosus. Furthermore, it has been of especial interest to study the mixing conditions of the residual blood of the heart both under physiologic conditions and also in those clinical conditions in which the heart is dilated. The influence of posture on the changes in the residual blood of the heart has been investigated as well. In addition, the changes in the type of the dilution curve in clinical conditions, such as hypotension and shock influenced by spinal anesthesia, have been gone into.

Duration of Specific Activity of Red Cells.—It has been asked if the red cells really retain their constant specific activity after injection for as long as one hour. In order to elucidate this point we have attacked the problem further by means of the following different experiments:

1. We have injected only the red cells. These, after having been separated from the active plasma, were washed twice with the patient's own plasma obtained prior to labelling.

2. We have injected only labelled plasma.

3. We have made double injections of labelled whole blood.

Fig. 2 shows the results of the first method. The diagrams show the change in the specific activity five to sixty minutes and then two, three, twenty, and twenty-four hours after the injection of only labelled red cells. It is remarkable that there is only a small amount of activity of the plasma from the fifth minute up to three hours after the injection of the labelled corpuscles. We suppose that the small quantity of activity of the plasma is due to the fact that we are not able to free the red cells from adherent active plasma even if they are washed twice with unlabelled plasma. The red cells have a constant activity up to

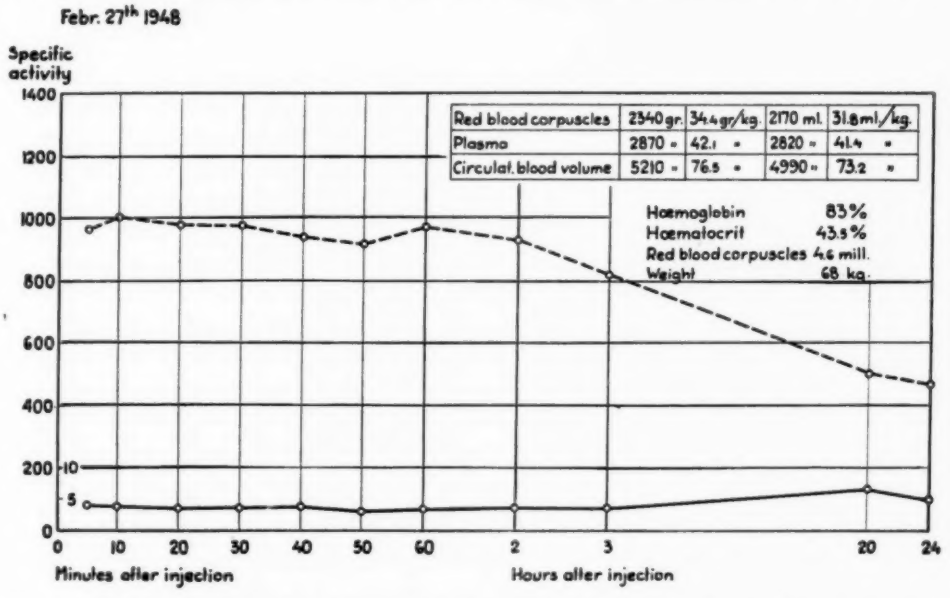

Fig. 2.—Specific activity of red blood corpuscles and plasma after injection of labelled blood corpuscles.

sixty minutes after the injection or even up to two hours after the injection, but they then rather slowly lose their activity. At the same time the slight activity of the plasma probably increases a little twenty to twenty-four hours after the injection of the active red cells.

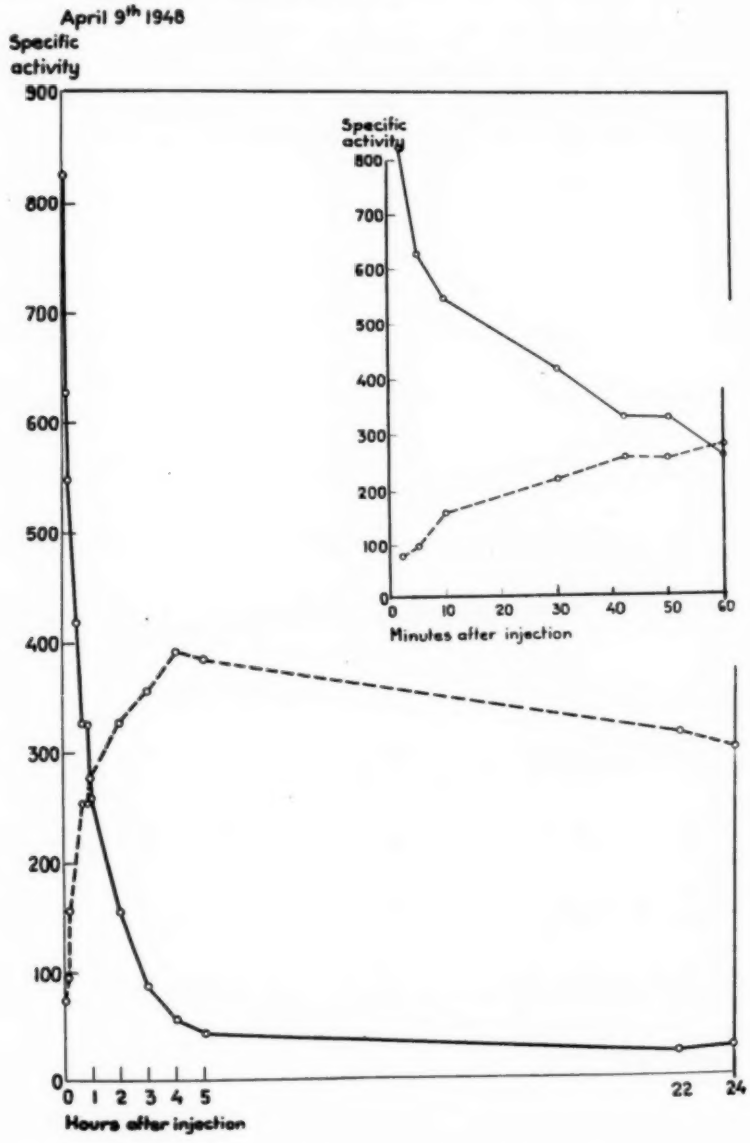

Fig. 3.—Specific activity of red blood corpuscles and plasma after intravenous injection of labelled plasma.

The second experiment of injecting only labelled plasma is instructive. From Fig. 3 one can see that even under these conditions the plasma activity decreases very rapidly up to three, four, or five hours after the injection and

that there still remains a minimal activity twenty-two and twenty-four hours after the injection. On the other hand, the red cells increase their activity for one to five hours after the injection of labelled plasma because radioactive phosphate enters the corpuscles. There is, as has been shown in the figure, probably a maximum labelling of the red cells about five hours after the injection; thereafter, up to twenty-two to twenty-four hours, a rather slow decrease of the activity of the red cells occurs. In the upper right hand corner of Fig. 3 the first part of the curve is enlarged to show the early changes in activity of the labelled red cells and the plasma more clearly. It is rather remarkable that the crossing point of these curves in two experiments in normal persons occurs about sixty minutes after the injection.

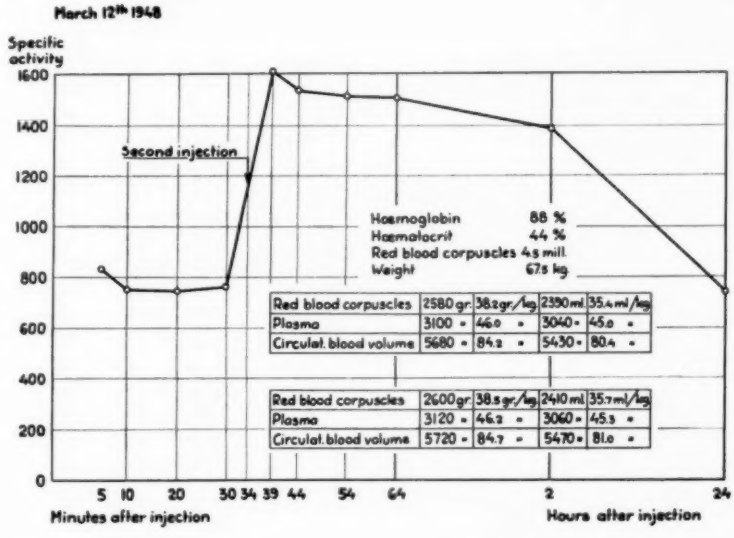

Fig. 4.—Specific activity of red blood corpuscles and plasma after double intravenous injections of labelled whole blood.

The results of the third experiment, in which double injections of labelled whole blood are made, is shown in Fig. 4. The second injection was made thirty-four minutes after the first one. The first part of the curve illustrates the specific activity of the red cells five to thirty minutes after the injection of labelled whole blood and shows that the activity is constant. After the second injection, made thirty-four minutes after the first one, the activity of the red cells is practically constant up to the sixty-fourth minute and then decreases, as has been shown before, rather slowly in twenty-four hours. In this way the second injection may be a control of the determination of the circulatory corpuscular volume, and the agreement between the two determinations in this example is very good. The difference in the weight of the red cells is only 20 grams.

*Determination of Residual Blood of Heart, Minute Volume, and Thoracic Pool of Blood.**—During the last three or four years we have tried to obtain an

*A full description of the method used will be published in the AMERICAN HEART JOURNAL.[19]

idea of the amount of the residual blood in the heart, the cardiac output, and the thoracic pool of blood. We have attempted to obtain these data mathematically from estimations of the dilution curve from the arterial blood.

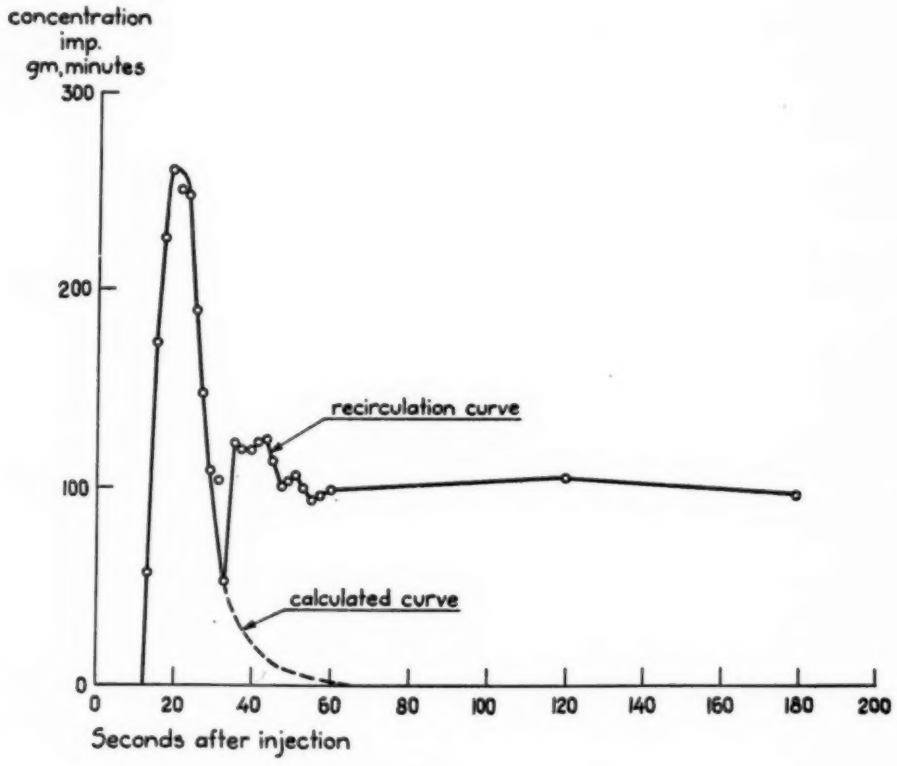

Fig. 5.—Dilution curve. Normal case.

Fig. 5 shows a typical dilution curve of a normal case. After the sample taken at the thirty-fifth minute, where the minimum of specific activity occurs, the calculated curve is dotted. From that point, however, the recirculation curve begins. From a curve of this type, as is shown in Fig. 5 and more schematically in Fig. 6, the cardiac output may be calculated by the aid of the following formula:

$$x = \frac{v_1 \cdot h_1 \cdot c_1'}{h \cdot \int_0^\infty c \cdot dt}$$

where x = the cardiac output
v_1 = volume of the injected labelled blood
c_1' = concentration of indicator of the injected sample

h_I = hematocrit of the injected blood

h = hematocrit of the circulating blood

$\int_0^\infty c\,dt$ = the area limited by the curve *DAGBJ* (Fig. 6) and the X axis. Of this area, the part *DAGH* must be determined graphically. The part below *GBJ* is determined by the formula:

$$\int_{t_H}^{\infty} c_o \cdot e^{-\lambda t}\,dt$$

where c_o and λ are constants which must be determined from the curve segment *GB*.

e = the base of the natural log system.

All the time units are in minutes. All volumes in liters.
An upper limit for the pool volume is $x \cdot \Delta t$
A lower limit for the pool volume is $\frac{x}{\lambda}$

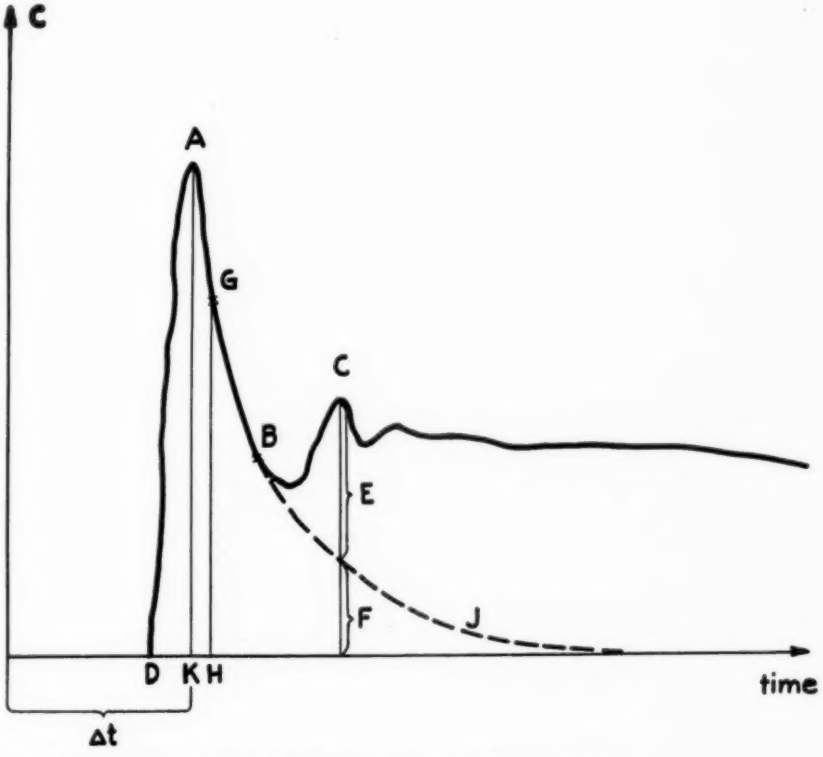

Fig. 6.—A dilution curve schematically represented. Discussed in text.

CONCLUSIONS

Detailed studies concerning the level of the corpuscular and plasma activity after (a) injection of labelled cells only, (b) injection of labelled plasma only, and (c) double injections of labelled whole blood show the following:

1. Injected labelled red cells remain constant in their activity for at least one hour after injection. The activity of labelled plasma, when given by itself, decreases very rapidly. On the other hand, the radioactive phosphate from the plasma enters very slowly into the corpuscles and reaches a maximum in the corpuscles about five hours after injection. It seems to be a normal finding that the activity of the red cells and also of the plasma is the same about sixty minutes after injection.

2. Double injections of whole blood, the second injection being given about thirty minutes after the first injection, give the same calculated blood corpuscular volume as determined from the first injection. This can be used as a control.

3. With the help of the injected labelled corpuscles it is possible to calculate the minute volume of the heart and the thoracic pool of blood from the dilution curve in the arterial blood.

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COMPLETE TRANSPOSITION OF THE AORTA AND A LEVOPOSITION OF THE PULMONARY ARTERY

Clinical, Physiological, and Pathological Findings

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THE clinical findings presented in the following case report represent a syndrome which we have seen not infrequently in recent years in the cardiac clinic of the Harriet Lane Home. This is, however, the first instance in which it has been possible to correlate the clinical findings with the autopsy findings. The case clarified the nature of the malformation and unfortunately demonstrated one of the most serious dangers of angiocardiography. Hence, the case is reported in detail.

CASE REPORT

P. A. W. (H. L. H. A-60186), a 5½-year-old white girl, was referred to the clinic for diagnosis of her cardiac abnormality.

The family history was noncontributory. The mother had not had German measles nor any rash or unexplained fever during her pregnancy. There was no familial history of congenital abnormalities.

The past history indicated that cyanosis was noted at birth and persisted throughout her life. At 3 weeks of age, a murmur was heard over the precordium. During infancy she gained weight slowly. At the age of 1 year she weighed 7.6 kilograms. Her development was also slow: she sat alone at 9 months and walked at 2 years. When about 3 years of age she frequently squatted down to rest, but soon outgrew the habit.

Physical Examination.—The temperature was 37° C., pulse 120, respiration 30, height 110 cm., weight 15.6 kilograms, and blood pressure 100/80. The child was an intelligent, moderately cyanotic, poorly developed girl who suffered from dyspnea at rest. There was suffusion of the conjunctivae. The lips and buccal mucous membranes were deeply cyanotic. The tonsils were small. The teeth were in good condition. The heart was slightly enlarged. The rhythm was regular. A systolic murmur was audible over the precordium which was definite but not loud; no thrill could be felt. The lungs were clear to percussion and auscultation. The liver and spleen were not palpable. The pulse in the femoral artery was of good quality. There was cyanosis and clubbing of the fingers and toes.

Laboratory Data.—The red blood cell count was 9.3 million. Hemoglobin concentration was 23.5 grams. The hematocrit was 77. Arterial blood analysis showed an oxygen content of 17.4 volumes per cent, oxygen capacity of 30.8 volumes per cent, oxygen saturation of 57 per cent, and carbon dioxide content of 25.8 volumes per cent.

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Presented before the Third Inter-American Cardiological Congress, Chicago, Ill., June 13-17, 1948.

Teleroentgenogram.—The heart was slightly enlarged. There was fullness of the pulmonary conus and the hilar markings were increased (See Fig. 1).

Fluoroscopy.—The findings in the x-ray film were confirmed and, in addition, fluoroscopy revealed faint expansile pulsations of the hilar shadows. Delineation of the esophagus with a barium-opaque mixture showed a left aortic arch and no evidence of left auricular enlargement.

Electrocardiogram.—There was a normal sinus mechanism, sinus tachycardia, normal P-R interval, high P waves in the second lead, right axis deviation, and right ventricular hypertrophy.

Clinical Impression.—The clinical findings were characteristic of an Eisenmenger complex in that there was cyanosis, clubbing, and polycythemia; the heart was slightly enlarged with x-ray evidence of fullness of the pulmonary conus and increased hilar shadows, which upon fluoroscopy showed faint expansile pulsations. However, the fact that cyanosis dated from birth made us suspect some totally different malformation.

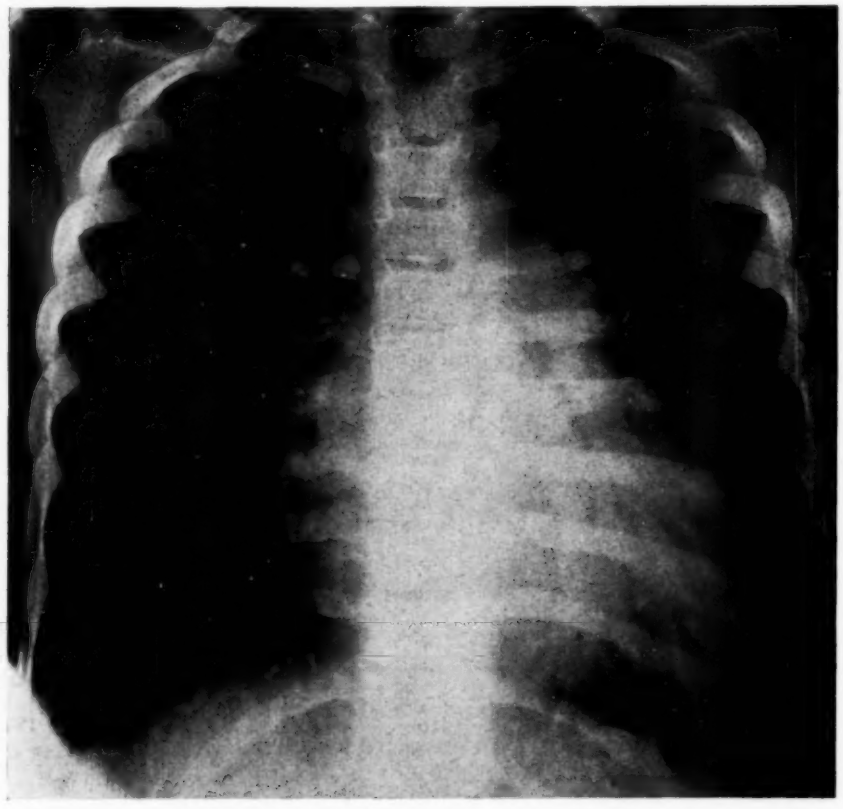

Fig. 1.—Teleroentgenogram of the chest, anterior-posterior position.

In Norway in the summer of 1947, one of us (H. B. T.) had been told of an infant with a similar clinical history. In this instance, examination of the heart showed an unusual anomaly of the great vessels: the aorta, which was abnormally small, arose from the right ventricle and the pulmonary artery was greatly enlarged and overrode the ventricular septum. For this reason, in the case under discussion, an overriding pulmonary artery was postulated, but, because of the

age of the patient and child's comparative well-being, the transposition of the aorta was not suspected.

Inasmuch as the diagnosis in this instance was obscure, the patient was referred to the physiological laboratory for special studies by one of us (R. J. B.) and to the x-ray department for angiocardiography.

Results of Physiological Studies.—Results obtained from the standard exercise test[1] showed that the oxygen consumed per liter of ventilation fell from 17 to 12 cubic centimeters. From this, it was inferred that the effective pulmonary blood flow through the lungs did not increase normally with exercise.

The results of cardiac catheterization are given in Fig. 2. It may be seen that the oxygen content of the right ventricular blood was significantly higher than that of the right auricle, indicating the presence of a ventricular septal defect. Of special interest was the finding that the oxygen content of the pulmonary arterial blood exceeded that of the right ventricular blood by 4.4 volumes per cent. The finding suggested admixture of oxygenated blood with right ventricular blood. A gradient of this magnitude between the right ventricular blood and the pulmonary arterial blood could have been the result of a ductus arteriosus, or of a communication between the pulmonary artery and the left ventricle through a high ventricular septal defect with the pulmonary orifice overriding the lower portion of the ventricular septum. The clinical findings, however, rendered unlikely the diagnosis of a patent ductus arteriosus as there was no continuous machinery-like murmur. Furthermore, the peripheral arterial oxygen saturation was only 57 per cent. It seemed almost certain that a large patent ductus arteriosus would increase the effective pulmonary blood flow sufficiently to raise the oxygen saturation of peripheral arterial blood to a higher level. It was, therefore, assumed that the pulmonary artery received oxygenated blood directly from the left ventricle.

Fig. 2 shows that the oxygen content of peripheral arterial blood was 7.6 volumes per cent less than that of the pulmonary arterial blood and 3.2 volumes per cent less than that of the right

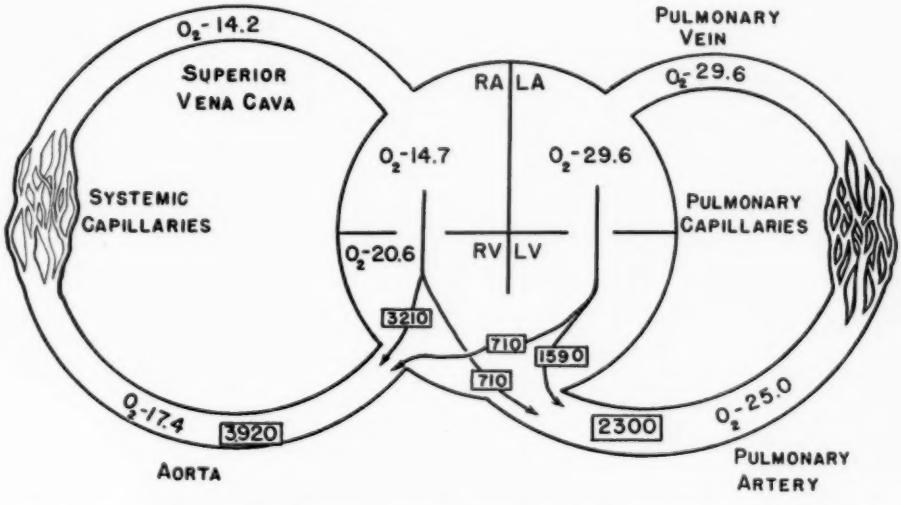

Fig. 2.—Diagram illustrating intracardiac hemodynamics. O_2 indicates oxygen content of the blood in volumes per cent. Oxygen content of the blood in pulmonary vein was calculated on the assumption that the blood was 96 per cent saturated.[2] Figures in boxes give volume of blood flow in cubic centimeters per minute per square meter of body surface. It may be seen that the large volume of the right auricular blood flows directly from the right ventricle into the aorta and only a small volume of blood passes into the pulmonary artery. This latter represents the effective pulmonary blood flow.

ventricular blood. This finding indicated that the aorta must receive a large quantity of unoxygenated blood. This could be the result of a high septal defect with the aorta overriding the ventricular septum or a complete transposition of that vessel. Although the latter possibility seemed likely, the physiological data alone were insufficient to establish the diagnosis. The pressures recorded in the pulmonary artery were 57/45 mm. of mercury; those in the right ventricle were 42/19 mm. of mercury (Fig. 3).

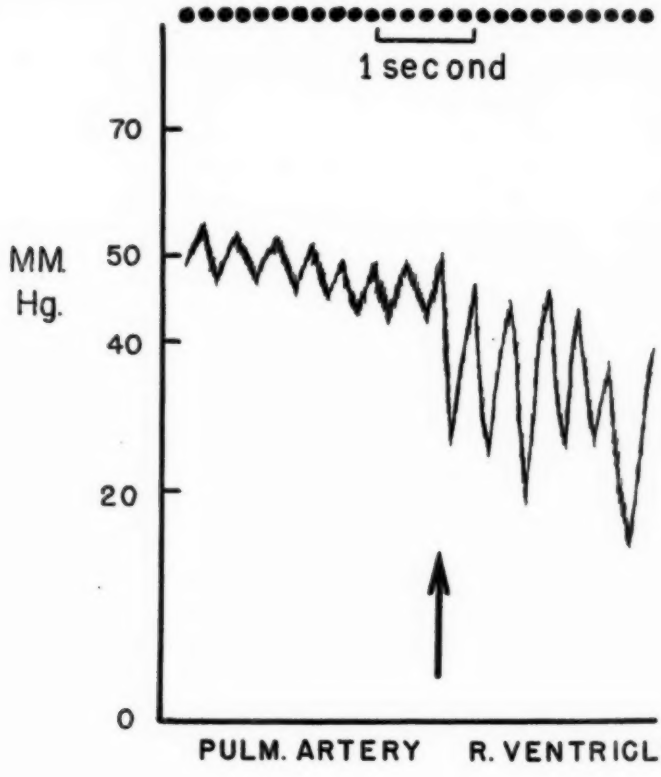

Fig. 3.—Continuous tracing of direct strain-gauge recording obtained in the pulmonary artery and in the right ventricle. The arrow indicates the point at which the tip of the catheter passes through the pulmonic valve into the right ventricle.

Angiocardiography.—After an initial test dose, the patient was given 19 c.c. of 70 per cent Diodrast intravenously through a canula and a series of eight films were taken in eight seconds. Thirty minutes later she was given another dose of 19 c.c. and a second series of eight films were taken. Because of a mechanical defect, no exposures were obtained. Therefore, fifteen minutes later, a third dose of 19 c.c. of Diodrast was injected and a series of eight films were photographed in eight seconds. There was no immediate reaction, but three minutes thereafter the child sat bolt upright and the heart stopped. All effort at resuscitation failed.

The angiocardiograms showed that the dye entered the right auricle and then the right ventricle; immediately thereafter the aorta was promptly visualized. Very little dye was seen in the pulmonary artery or the lungs. The circulation of the dye could not be traced further. The second series of films taken in the lateral position showed that the aorta appeared to arise from the anterior portion of the right ventricle. Again, the circulation of the dye could not be traced into the lungs, nor to the left side of the heart.

Final Clinical Diagnosis.—The physiological studies and angiocardiograms indicated a transposition of the great vessels. The x-ray and fluoroscopic findings indicated that such was not the case in that the pulmonary artery appeared to arise from the right ventricle.

Autopsy (No. 21039, Performed by Dr. Edmund Novak).—The chief interest centered about the heart. It weighed 180 grams. The right auricle was not greatly enlarged. The superior vena cava and the inferior vena cava opened into it in the normal fashion. The foramen ovale was completely covered by a valve, but there was probe patency of the valve for a distance of 1.0 cm. along its margin. The tricuspid valve, which was slightly thickened, opened into the right ventricle. That chamber was tremendously hypertrophied; its wall measured 1.5 cm. in thickness. The pulmonary artery arose approximately in its normal position. The aorta was transposed; it arose entirely from the right ventricle. The aortic orifice lay adjacent to the pulmonary orifice and to the ventricular septum as shown in Figs. 4 and 5. The aortic valve had three cusps and the coronary arteries were given off from the aorta in the normal manner. The aortic ring meas-

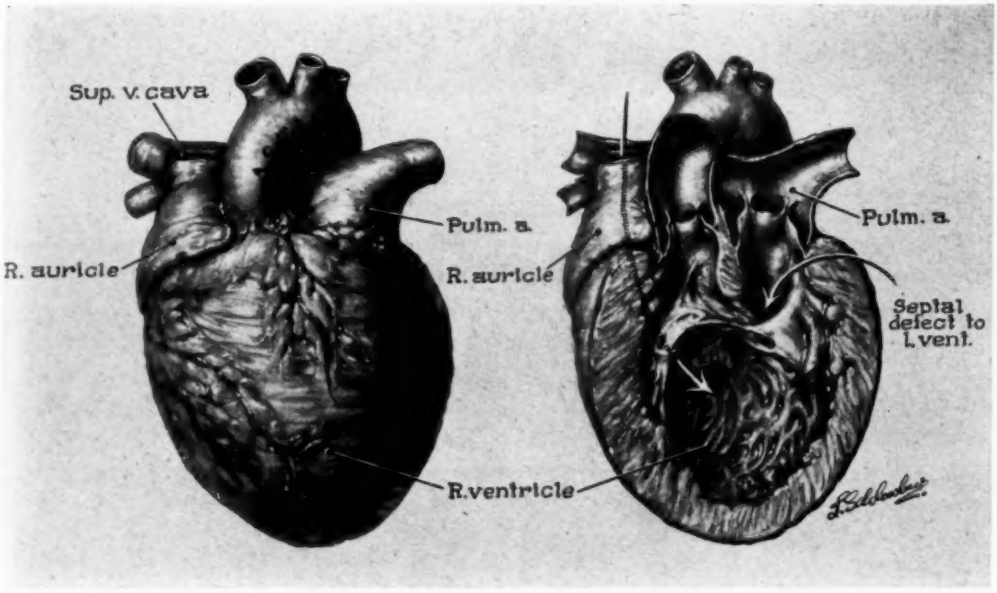

Fig. 4.—Drawing of the heart showing size and position of the aorta and pulmonary artery and their relation to the septal defect.

ured 3.5 cm. in circumference. The aorta and its branches appeared to be normal. The maximum circumference of the ascending aorta was 4.0 centimeters. At the base of the ventricular septum, the septal wall was defective for a distance of 1.2 cm. and the defect extended downward toward the apex for approximately 0.6 centimeter. The superior portion of the ventricular septum deviated to the right to such an extent that the pulmonary orifice overrode the septal defect by a few millimeters. From the upper margin of the ventricular septum close to the defect, a muscular ridge extended forward to the outer wall of the right ventricle. This ridge separated the aorta from the pulmonary artery. Consequently, the aorta arose entirely from the right ventricle and only the pulmonary orifice overlay the ventricular septum. Thus, the pulmonary artery not only received blood from the right ventricle, but also received blood directly from the left ventricle. The pulmonary artery and its branches were greatly dilated. The pulmonary orifice measured 5.8 cm. in circumference and the main pulmonary artery above the ring had a circumference of 6.5 centimeters. The left main branch measured 4.0 cm. in circumference; the right

branch was approximately the same size. The pulmonary arterial wall was thicker than normal; its intima, however, was smooth. The ductus arteriosus was closed. The examination of the myocardium showed that the fibers were hypertrophied but there were no infarcts and no thrombi. The coronary arteries appeared to be normal. The bronchial arteries were not enlarged.

The lungs were air containing and showed no evidence of pneumonia or pulmonary infarcts; all the pulmonary vessels were patent. Microscopic examination of the lungs revealed occasional thrombi, some of which were in the process of recanalization. Many of the small pulmonary arterioles showed diffuse, intimal proliferation which rendered these vessels extremely narrow. The lesion appeared to be sufficient to account for the increased resistance in the pulmonary vascular bed. In addition, the pulmonary alveoli showed areas of emphysema and areas of atelectasis.

The liver showed marked congestion. The spleen was enlarged and showed evidence of congestion; it weighed 140 grams. There were many small accessory spleens. The kidneys were normal except for congestion; each weighed 80 grams. The cortex and medulla were well defined. The pelvis and ureters were not remarkable. There was a diffuse hemorrhage in the thymus.

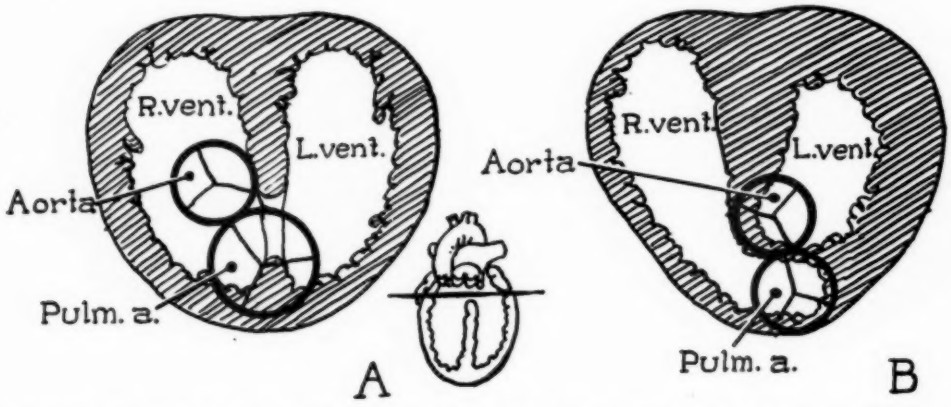

Fig. 5.—Cross section of the heart illustrating the relation of the aorta and the pulmonary artery to the ventricular septum, *A*, in this malformation and *B*, in the normal heart.

Final Anatomical Diagnosis.—Transposition of the aorta. Dilatation and slight displacement of the pulmonary artery. Ventricular septal defect. Foramen ovale covered by a valve, but not completely sealed. Dilatation and hypertrophy of the right ventricle. Extreme thickening and intimal proliferation of the pulmonary arterioles and small arteries. Occasional recanalization of thrombi in the pulmonary arterioles. Splenomegaly. Patchy emphysema and atelectasis. Acute congestion of the lungs and viscera. Diffuse hemorrhage in the thymus.

DISCUSSION

Autopsy showed that the aorta was transposed and the pulmonary artery arose primarily from the right ventricle, but overrode the ventricular septum and received blood directly from both ventricles. This malformation is tabulated by Pernkopf[3] as one of the possible combinations which may occur in transpositions of the great vessels.

The malformation was similar to the one the author had seen in Norway, except that the aorta was not abnormally small and the ventricular septal defect was larger than in the Norway specimen. These two factors rendered the malformation more readily compatible with life.

This malformation produces a syndrome which is clinically similar to that associated with an Eisenmenger complex. In both conditions the pulmonary artery arises from the right ventricle; in both, the contour of the heart in the x-ray film shows fullness of the pulmonary conus. Both have large pulmonary arteries, which upon fluoroscopy usually show expansile pulsations. In both malformations the heart is but slightly, if at all, enlarged; both have a systolic murmur; both show evidence of right axis deviation and right ventricular hypertrophy. Both conditions are compatible with life for a number of years. In both, the habit of squatting is either entirely absent or of short duration. The outstanding clinical difference between this malformation and the Eisenmenger complex is that in the former, cyanosis dates from birth, whereas the late development of cyanosis, at or about the time of puberty, is characteristic of the Eisenmenger complex. Both conditions lead to polycythemia and clubbing of the extremities which, however, occur at a later date in patients with an Eisenmenger complex than with this malformation.

Anatomically, this malformation differs from an Eisenmenger complex in that the aorta is not dextroposed; that is, it does not arise from the left ventricle and partially override the ventricular septum, but it is *transposed* and arises entirely from the right ventricle. Furthermore, it is the pulmonary artery, not the aorta, which overrides the ventricular septum.

The origin of the aorta from the right ventricle means that the blood from the right ventricle is pumped directly into the aorta; this readily explains the early appearance of cyanosis. Indeed, the only oxygenated blood to reach the aorta is that which is shunted from the left ventricle through the septal defect into the right ventricle. Inasmuch as the pulmonary artery overrides the ventricular septum, blood from the left ventricle is readily directed into the pulmonary artery.

Functionally, this malformation closely resembles the malformation in which both the aorta and the pulmonary artery arise entirely from the right ventricle and the septal defect lies beneath the pulmonary artery. This last mentioned malformation is also mentioned by Pernkopf[3] and has been classified by some as an Eisenmenger complex, but is totally different from the malformation originally described by Eisenmenger and, to use Dr. Maude Abbott's words, "is not to be confused with an Eisenmenger complex." Therefore, the authors feel that the term "Eisenmenger complex" should be limited to the type of malformation originally described by Eisenmenger and that the combination of a transposed aorta with a pulmonary artery which arises from the right ventricle and partially overrides the ventricular septum represents a separate clinical and pathological entity. Furthermore, the malformation, in which both great vessels arise from the right ventricle and in which the septal defect is adjacent to the posterior margin of the pulmonary orifice, is functionally more closely related to the malformation under discussion than to the Eisenmenger complex.

The origin of the aorta from the right ventricle means that venous blood is directed into the aorta and, consequently, the oxygen saturation of the arterial blood is abnormally low. Exercise causes a further fall in the oxygen saturation

of the arterial blood and a fall in the oxygen consumption per liter of ventilation. The latter finding is similar to that which occurs in a patient with a tetralogy of Fallot and, not infrequently, with a complete transposition of the great vessels, but is contrary to that which occurs in a patient with an Eisenmenger complex.

Cardiac catheterization reveals a high pressure in the right ventricle and a markedly higher oxygen content in the right ventricle than in the right auricle (Fig. 2). Therefore, if the pulmonary artery is not catheterized, the findings are similar to those in a tetralogy of Fallot. If the pulmonary artery is catheterized, the pulmonary pressure will be found to be high and the oxygen content in the pulmonary artery will be higher than that in the femoral artery.

The intracardiac hemodynamics of this patient are illustrated in Fig. 2. Her oxygen consumption was 105 c.c. per minute per square meter of body surface. As shown in Fig. 2, the systemic flow was 3,920 c.c. per minute per square meter of body surface and the pulmonary artery flow was 2,300 c.c. per minute per square meter of body surface. Thus, the systemic flow exceeded the pulmonary artery flow by 1,620 cubic centimeters. Both were calculated according to formulas published in a previous communication.[2] The effective pulmonary blood flow is the quantity of blood which, after having been returned to the right auricle from the body, is eventually aerated in the lung.[2] In this patient, it will be represented by the volume of mixed venous blood which enters the pulmonary artery from the right ventricle. Consequently, it can be calculated from the oxygen content of the blood in the right auricle and the oxygen content of the blood returned to the left auricle.[2] In this instance, the effective pulmonary blood flow was found to be 710 cubic centimeters. This means that, although the volume of the pulmonary blood flow is 2,300 c.c., only 710 c.c. are mixed venous blood; the remainder is arterial blood which is recirculated through the lungs. Furthermore, in order to keep the pulmonary flow at its calculated constant value, 710 c.c. must be shunted from the left ventricle into the aorta. Since this represents the oxygenated component of the blood supplied to the systemic circulation, it represents the effective systemic flow. The remaining 3,210 c.c. of the systemic flow is mixed venous blood from the right auricle which passes into the right ventricle and is pumped out into the aorta and recirculated through the body.

The relatively small volume of blood entering the aorta from the left ventricle furnishes the only means by which oxygenated blood reaches the body. This explains the low oxygen saturation in the peripheral arterial blood and the severe cyanosis. Consequently, any diminution of this volume may have dangerous consequences.* This may explain the fatal outcome of angiocardiography.

*It is our belief that any condition in which the injection of Diodrast decreases the supply of oxygen to the individual is extremely dangerous. The danger of angiocardiography in pulmonary arteriovenous aneurysms is well known.[4] Under such circumstances, the dye is laked in the aneurysms and interferes with the exchange of oxygen in the lungs. Angiocardiography also proved fatal in a man with a cor pulmonale in whom the pulmonary arteriolar disease caused difficulty in the circulation of the blood through the lungs and in the oxygenation of the blood in the lungs. Recently, a child with an extreme pulmonary stenosis and no ventricular septal defect died after the injection of a single dose (9 c.c.) of Diodrast. In this instance, the orifice into the pulmonary artery was only 1.0 mm. in diameter and the expulsion of dye through this tiny orifice cut off the entire blood supply to the lungs and thereby deprived the child of its sole supply of oxygenated blood.

In this malformation, the increased pressure in the right side of the heart may have blocked the supply of oxygen to the systemic circulation.

In this instance, the rapid injection of the Diodrast into the superior vena cava raised the pressure in the right side of the heart and, consequently, decreased the left-to-right shunt. For this reason, angiocardiography was exceptionally dangerous for this patient. Furthermore, angiocardiography did not clarify the nature of the malformation and therefore is not necessary to establish the diagnosis.

SUMMARY

A new clinical syndrome is described. The malformation consists of a transposed aorta, a large pulmonary artery which arises primarily from the right ventricle and partially overrides the ventricular septum, a high ventricular septal defect, and right ventricular hypertrophy.

Clinically, in this instance the heart was but slightly, if at all, enlarged; there was a systolic murmur and thrill. Cyanosis dated from birth. Clubbing of the extremities developed at an early age. The red blood cell count, the level of the available hemoglobin, and the hematocrit reading were increased. The electrocardiogram showed evidence of right ventricular hypertrophy. The x-ray films of the heart showed fullness of the pulmonary conus and increased hilar shadows. Upon fluoroscopy, the pulmonary vessels showed faint expansile pulsations. The oxygen saturation of the arterial blood was abnormally low and fell still further with exercise.

In brief, the clinical syndrome associated with this malformation resembled that of an Eisenmenger complex, except that cyanosis dated from birth.

The two conditions showed a further difference in that, in the Eisenmenger complex, exercise causes an increase in the consumption of oxygen per liter of ventilation, whereas in this malformation, exercise causes a decline in the oxygen consumption per liter of ventilation.

Intracardiac catheterization studies revealed a higher oxygen content in the pulmonary artery than in the femoral artery. It is probable that the volume of blood which entered the pulmonary artery from the right ventricle was equal to that directed from the left ventricle into the aorta. The extensive intimal changes in pulmonary arterioles appeared to be sufficient to account for the increased resistence in the pulmonary vascular bed.

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STUDIES ON THE CORONARY CIRCULATION

IV. The Effect of Shock on the Heart and Its Treatment

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SHOCK is a common, dreaded complication of coronary artery occlusion. It has been shown that in coronary artery occlusion, patients who develop shock have a much poorer prognosis than those who do not. Recent studies have also demonstrated the deleterious effects of shock on the myocardium.[1-7] In acute coronary artery occlusion, physicians look upon the development of pallor, weakness, sweating, fast weak pulse, poor heart sounds, and gallop rhythm as ominous signs. Most of our knowledge of shock is a result of the study of traumatic shock. Thus, for example, the mechanism and treatment of shock accompanying burns is infinitely better understood than that with coronary artery occlusion. A large percentage of patients die as a result of shock after coronary artery occlusion, and, except for a few poorly studied procedures, there is no well-defined treatment for this type of shock. Thus, the subject was considered worthy of investigation.

At present, the usual treatment for the patient in shock from coronary artery occlusion is heavy sedation, oxygen, coronary dilator drugs, and watchful waiting. Many[8,9,10] believe that shock after coronary occlusion is a "compensatory" phenomenon which reduces the work of the heart. They therefore believe that it should not be treated. From the evidence of the investigations to be presented, we feel that it is probably just as important to treat the shock which follows coronary artery occlusion as that which follows surgery or trauma.

Previous investigations from this laboratory with the use of radioactive red blood cells, fluorescein, and microsphere perfusion have demonstrated that after coronary occlusion blood enters the ischemic region of myocardium through interarterial anastomoses of arteriolar size.[11,12] These investigations also revealed that the collateral blood supply to the epicardial portion of ischemic myocardium

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From the Institute for Medical Research, Cedars of Lebanon Hospital, Los Angeles, Calif.
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Motion pictures of these experiments were presented at the conventions of The American Heart Association, Atlantic City, June 6, 1947, The American College of Physicians, San Francisco, April 23, 1948. The Third Inter-American Cardiological Congress, Chicago, June 13-17, 1948. The American Heart Association, Chicago, June 19, 1948, and The American Medical Association, Chicago, June 21-25, 1948.
Photographic reproductions published in this article were taken from these films. The motion pictures, of course, demonstrate the phenomena more clearly than still photographs.

was much better than that to the endocardial portion and that the collateral circulation of the right ventricle was better than that of the left ventricle. The numerous anastomoses between the normal coronary arteries of a dog have been visually demonstrated by cinematographic studies of the beating dog's heart by the injection of air or colored viscid solution into the ligated anterior descending branch of the left coronary artery 3.0 to 6.0 cm. proximal to the tie, and also by the injection of fluorescein into the cannulated anterior descending artery.[13]

It was the purpose of this study to determine the effect of shock on the heart. Therapeutic procedures are suggested as a result of the extensive data that have been obtained.

PART I. EXPERIMENTAL STUDIES OF THE EFFECT OF SHOCK ON THE CORONARY CIRCULATION OF DOGS

Experiment I. The Effect of Shock on the Collateral Circulation Studied by Means of the Radioactive Red Blood Cell Technique.—

Method: Radioactive erythrocytes are easily prepared by the incubating of red blood cells with phosphorus 32. After repeated centrifugation and washing of the cells, they are a useful tool for studying the coronary circulation. By knowing the amount of radiation a known volume of radioactive red blood cells emits, one can easily and accurately determine the volume of blood per gram of tissue by means of a Geiger counter. Furthermore, the heart of an animal injected with radioactive erythrocytes can be placed against a piece of unexposed x-ray film and a radioautograph can be prepared. A shadow is produced by the beta rays from the phosphorus in the red blood cells and the intensity of the shadow is proportional to the number of red cells at any particular area. Details of this method and the results in dogs with coronary occlusion and normal blood pressure have already been presented.[12]

Nine dogs were anesthetized with intravenous Nembutal. Artificial respiration was maintained by means of a tracheal catheter, and blood pressure was recorded by means of a mercury manometer connected to a cannula in the femoral artery. The chest and pericardium were opened and the anterior descending artery was ligated 1.0 to 3.0 cm. from its origin. The blood pressure was lowered to severe shock levels by hemorrhage from the femoral artery or by ventricular fibrillation, after which the radioactive red blood cells were injected intravenously and in the same quantity and manner as in the previous experiments. The hearts were stopped instantly by a freezing mixture of methyl cellosolve in carbon dioxide snow being poured on them one to four minutes after the injection of radioactive erythrocytes. The hearts were removed and opened by Schlesinger's technique. Determinations of the distribution and concentration of the red blood cells in nonischemic and ischemic myocardium were made by means of Geiger counts and radioautographs.

Results: The concentration of radioactive red blood cells in the ischemic region was markedly reduced on both the endocardial and pericardial surfaces of the hearts of dogs in shock. This is in contradistinction to results obtained in dogs with coronary artery ligation and normal blood pressure. In the hearts of

such dogs the quantity of radioactive red blood cells in the pericardial part of the ischemic myocardium was equal to that in the nonischemic muscle. In Fig. 1, a radioautograph of the pericardial surface of the heart of a dog in shock demonstrates this finding. Even more important is the fact that in the shocked dogs the quantity of radioactive red blood cells in control regions of myocardium was markedly diminished when compared with the quantity of cells in control regions

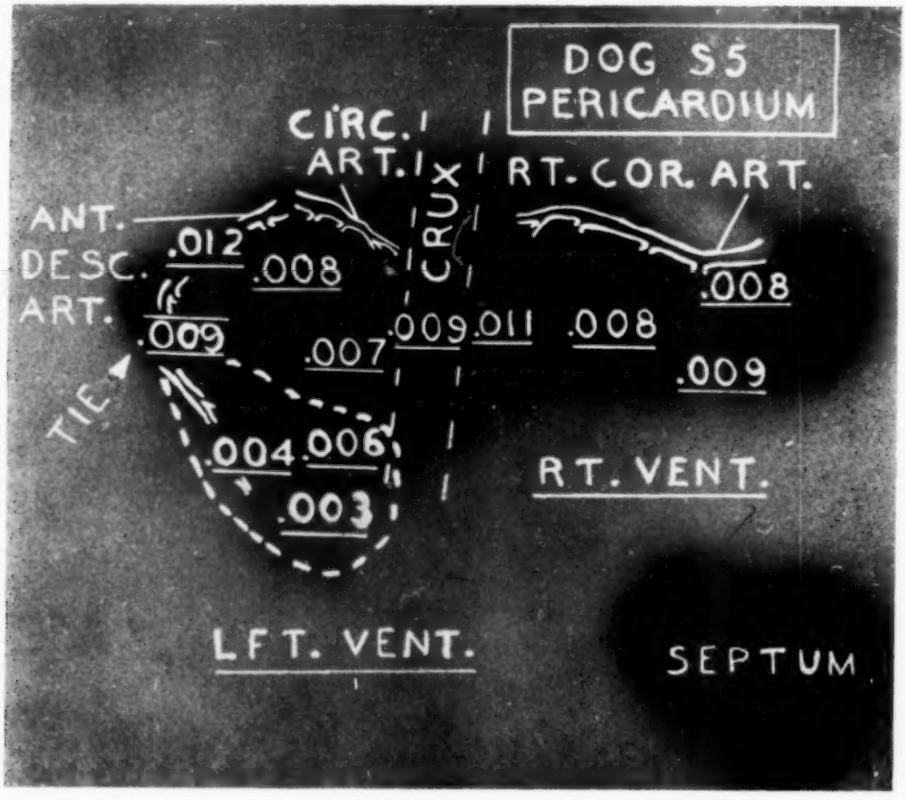


Fig. 1.—Radioautograph of heart of dog in shock with low blood pressure. Anterior descending coronary artery ligated. The figures indicate the volume of blood per gram of tissue as determined by Geiger counts. Note significant reduction in concentration of radioactive red blood cells in ischemic region outlined by dotted line.

of animals with normal blood pressure (Fig. 2). These results indicate that after shock the general coronary blood flow is markedly reduced. The collateral blood flow through intercoronary anastomoses is still more markedly decreased because of lowering of the interarterial pressure gradient. Opdyke and Foreman[14] also found that the coronary flow was reduced in shock.

Experiment II. Fluorescein Studies Showing the Effect of Shock on the Coronary Circulation.—

A. *Coronary Arteries Patent; Blood Pressure Lowered*: We have shown previously that the coronary circulation can be visually demonstrated in the

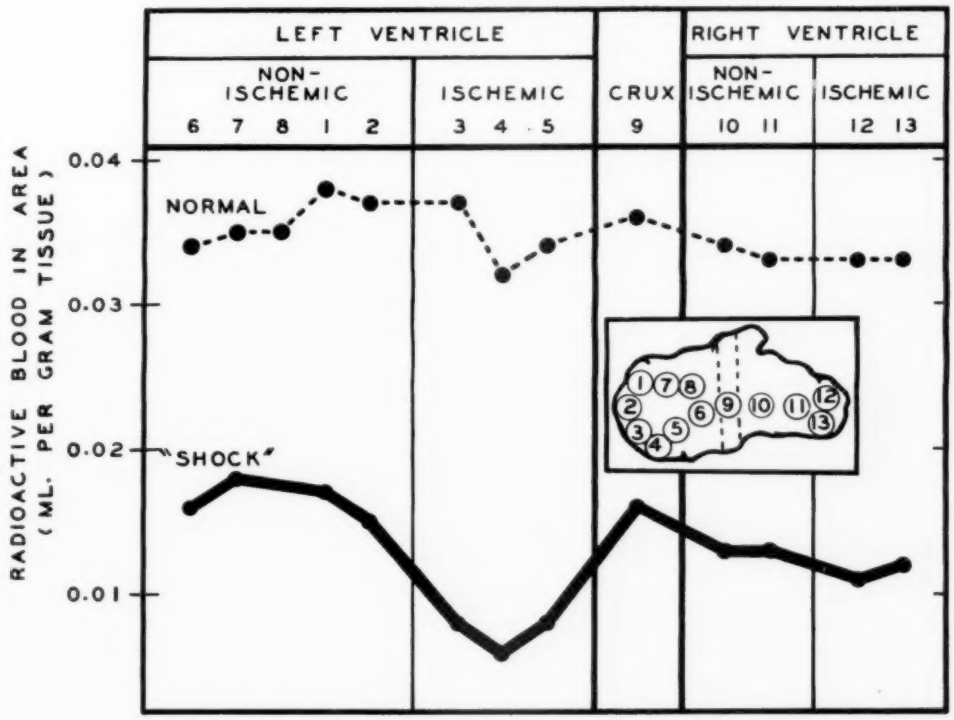


Fig. 2.—The average concentration of radioactive blood on the pericardial surface of hearts of twelve dogs with normal blood pressure is compared with that of nine dogs in shock with low blood pressure. Not only is the concentration of blood in the ischemic myocardium of "shock" dogs reduced, but more significant is the reduction in concentration of blood throughout the "shock" heart.

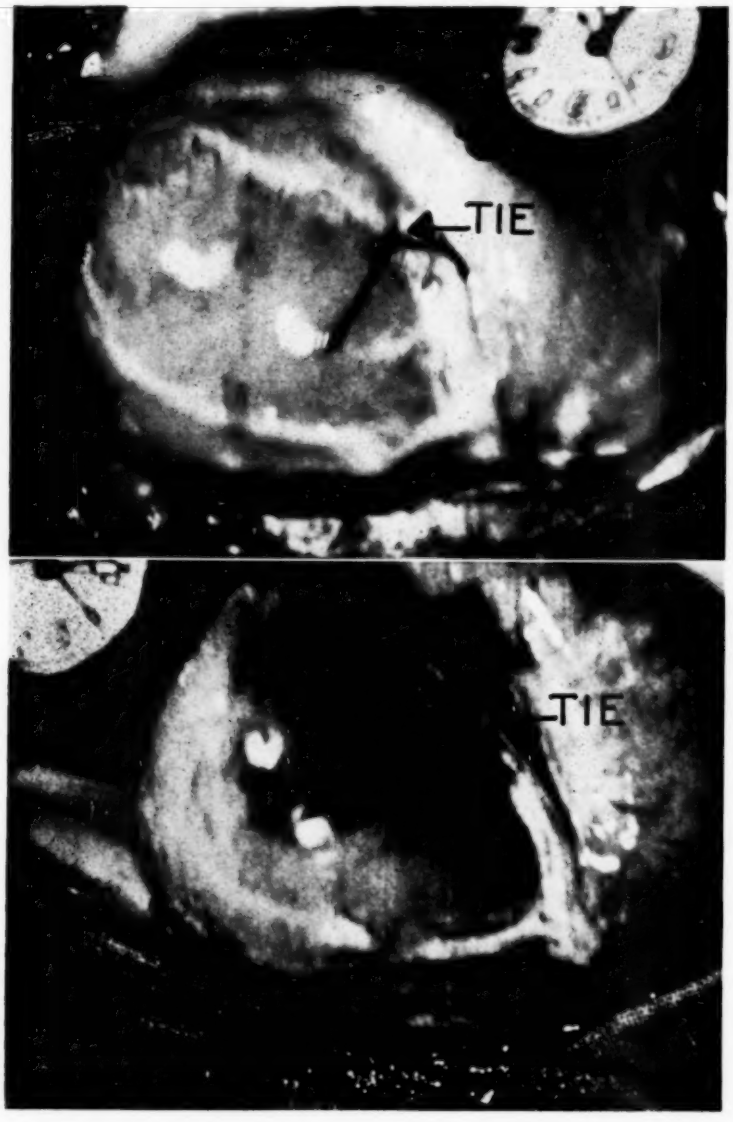
beating dog's heart by slow motion pictures (fifty frames per second) taken under special lighting which allows intravenously injected fluorescein to become visible. In animals with normal blood pressure, fluorescein appeared in the coronary arteries rapidly (within four to seven seconds) and in the next few seconds the entire heart became intensely fluorescent. This experiment was repeated on four dogs with low blood pressure induced by hemorrhage.

The appearance time of the fluorescein was greatly delayed, taking more than thirty-five seconds, and the rate of accumulation of fluorescein in the myocardium was greatly decreased. This was a visual de nonstration of the diminution of the coronary blood flow in shock.

B. *Coronary Arteries Ligated; Blood Pressure Lowered*: It was shown previously in dogs with normal blood pressure and with ties in the middle of the anterior descending artery that fluorescein rapidly filled the ischemic region from contiguous areas.[9] The ischemic region generally became intensely fluorescent one to two seconds after the control region (Fig. 3,*A*). The experiment was repeated in six control dogs after the blood pressure had been reduced by hemorrhage as described in Experiment II,*A*.

Within thirty-five seconds, fluorescein appeared in all parts of the myocardium except that supplied by the ligated artery. In the latter region, it appeared after forty-five seconds but with much less intensity (Fig. 3,*B*).

A.



B.

Fig. 3.—*A*, Dog's heart with anterior descending coronary artery ligated. Blood pressure is normal. Photograph taken twenty-three seconds after fluorescein was injected into femoral vein demonstrates that fluorescein has completely filled the ischemic as well as the nonischemic myocardium via collateral circulation. In these black and white photographs, fluorescence appears white.

B, Dog's heart, anterior descending coronary artery ligated. Blood pressure is reduced by hemorrhagic shock. Photograph, taken eighty-six seconds after injection of the fluorescein, demonstrates that the myocardium supplied by the ligated vessel is only partially filled with fluorescein.

Experiment III. Effect of Shock on Myocardial Noncontractility.—

By means of slow motion pictures, it has been shown that the ischemic myocardium ceases to contract within three to four seconds after the coronary artery is ligated. This phenomenon, which has been known for many decades, has been studied by Tennant and Wiggers[15] and more recently in our laboratory.[16] We have done an extensive investigation on noncontractility in the ischemic region after coronary artery ligation.[16] Sometimes this phenomenon, which we have termed "ballooning," occurs only in late systole, but in other instances the ischemic region balloons during the entire systolic phase. After relatively small coronary arteries are ligated, the ballooning may not occur at all or may dis-

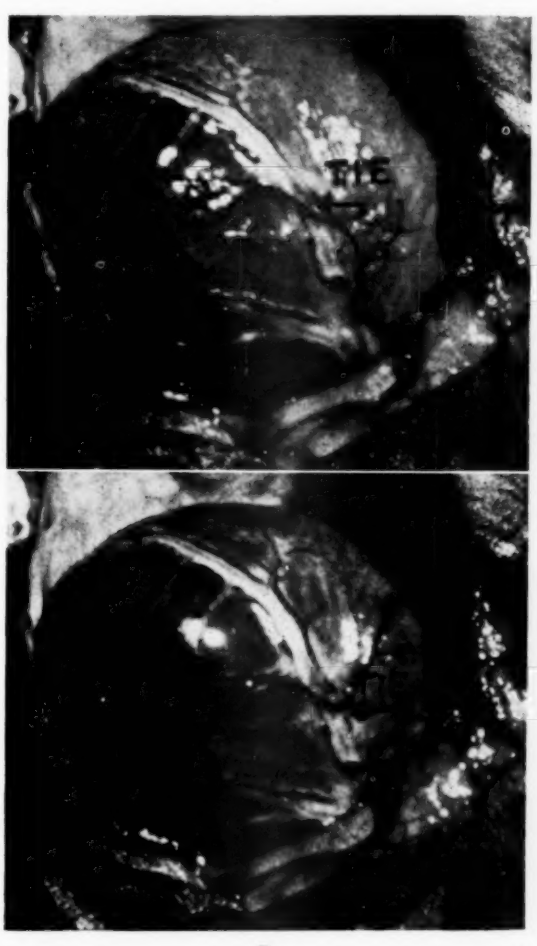


Fig. 4.—*A*, Dog's heart with anterior descending coronary artery ligated. Blood pressure is normal. Photograph taken in maximum systole demonstrates that the myocardium is contracting normally.

***B*, Same heart. Blood pressure now reduced by hemorrhagic shock. The myocardium supplied by the ligated artery now "balloons" outward in systole.**

appear within one minute and then may come and go for unknown reasons. After ligation of large vessels, the ischemic region balloons more consistently. We have observed this inconstancy of ballooning in human subjects with coronary occlusion by means of roentgenkymograms.[16]

Method: Motion pictures were taken during and after ligation of the anterior descending artery in six dogs with normal blood pressure. The blood pressure was then reduced by hemorrhage to very low levels.

Results: The following significant changes occurred as a result of the low blood pressure (Fig. 4,*A* and *B*):

1. The ballooning became much more extensive in area and degree.
2. Cyanosis of the ischemic area became marked.
3. If ballooning had disappeared spontaneously, it reappeared and became more marked.
4. If there was only late systolic ballooning and not full systolic ballooning, it now occupied the full phase of systole.

Experiment IV. The Effect of Transfusion on Myocardial Noncontractility of Dogs With Coronary Artery Occlusion and Shock Blood Pressure Levels.—

In these experiments the blood was heparinized upon withdrawal and after fifteen to twenty minutes was administered intravenously into the same animals, raising the blood pressure to the prehemorrhage level. Motion pictures were again taken of the same hearts after transfusion. It was found that ballooning became less intense or disappeared entirely and the cyanosis also diminished or disappeared (Fig. 5,*A* and *B*).

Experiment V. Effect of Coronary Insufficiency on the Heart.—

In order that the effect of shock upon coronary sclerosis might be studied, the condition was simulated experimentally by constriction of the coronary arteries.

A. *Animals With Normal Blood Pressure*: The coronary arteries of six dogs were constricted by a ligature placed around the artery and a narrow glass tube about 0.25 mm. in diameter. The tube was then removed. It is estimated that, by this technique, the lumen of the artery was reduced at least 50 per cent, and in most cases, much more. For assurance that the artery was still patent fluorescein was injected into the femoral vein. If fluorescein entered the area supplied by the constricted artery as promptly as it entered the control areas, it was evident that the lumen was patent.

In view of the obvious clinical importance of coronary insufficiency and myocardial noncontractility, first we shall describe its effect on animals with normal blood pressure.

During the process of tying the artery around the glass cannula, the ischemic myocardium ballooned; but a few seconds after the glass rod was removed, the

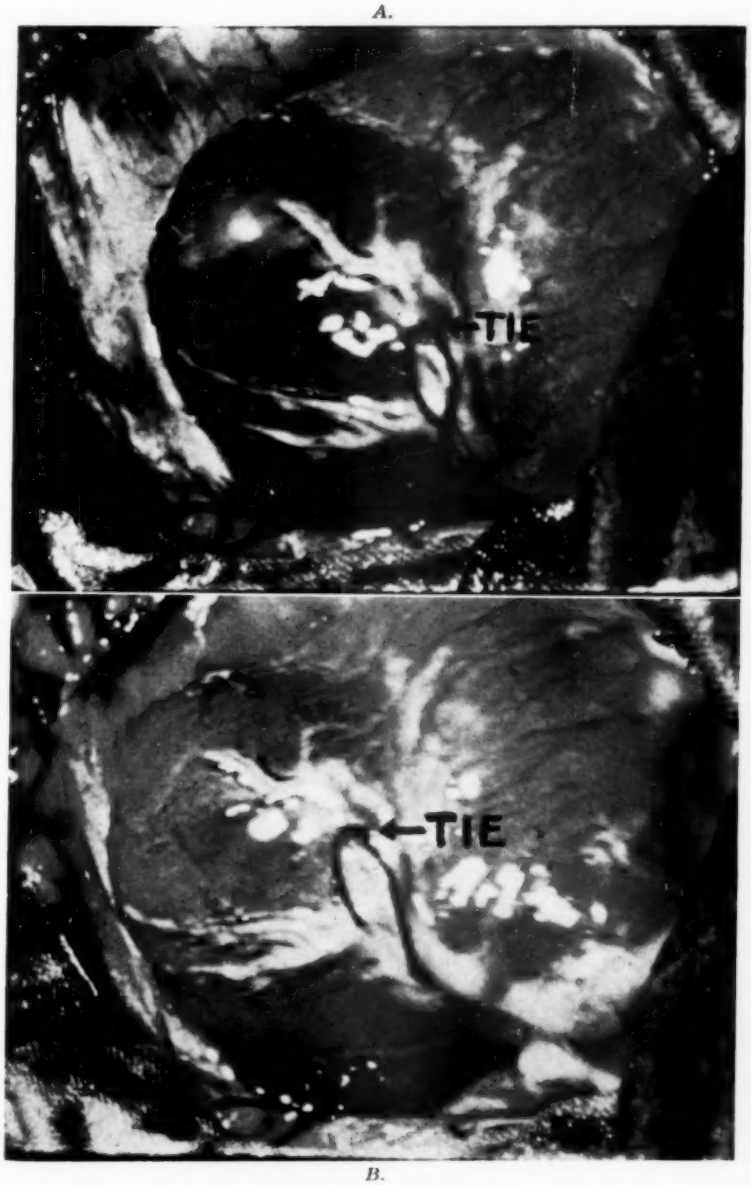


Fig. 5.—*A*, Dog heart with anterior descending coronary artery ligated. Blood pressure reduced by hemorrhage. Photograph taken in maximum systole demonstrates that the ischemic myocardium is cyanosed and "balloons" outward (outlined by broken line).

B, Same heart as in *A*. Blood pressure now restored to normal by transfusion. The photograph taken in maximum systole demonstrates that the ballooning has disappeared and that the myocardium again contracts normally.

region supplied by the partially constricted artery resumed normal contractions and its appearance resembled that of the region before the tie was made. There was no cyanosis, and the region supplied by the constricted artery appeared to have a normal blood supply since fluorescein entered this region as rapidly and with as much intensity as the surrounding control regions.

This observation with fluorescein indicates that the circulation to the region supplied by the partially occluded artery is only slightly or not at all impaired. It was shown that when the lumen of the vessel is greatly narrowed, the blood supply may still be normal as determined by fluorescein filling. It must be concluded that arterial dilatation occurs and increases the blood flow to this region. Thus, under normal circumstances, with normal blood pressure and without excessive work, coronary narrowing is compensated for by arterial vasodilatation which maintains adequate blood flow and preserves myocardial contractility.

In view of the widespread incidence of coronary sclerosis with narrowing of the coronary arteries, the clinical significance of this finding is evident.

B. *Animals With Reduced Blood Pressure and Constriction of the Coronary Artery*: In the animals just described, the blood pressure was reduced by hemorrhage, and slow motion pictures were again taken. It was found that the region which was previously nonischemic and contracted well now ballooned in systole and became cyanotic.

C. *Effect of Transfusion in Coronary Insufficiency*: After the intravenous administration of heparinized blood, as described in the previous experiment, the contractility returned, the cyanosis disappeared, and the heart again appeared normal in all respects.

It is obvious that although the blood supply and contractility of the myocardium were normal while the blood pressure was normal, reduction in blood pressure caused a diminution in blood flow with loss of contractility. The deleterious clinical effect of low blood pressure on patients with coronary sclerosis and the therapeutic effect of agents which raise blood pressure, a clinical corollary of this experiment, will be discussed later.

Experiment VI. Electrocardiographic Changes After Hemorrhagic Shock.—

In order to simulate the effect of shock on the electrocardiograms of patients with coronary sclerosis, constricting ties, as previously described, were placed on the anterior descending branch of the coronary artery in two dogs, the mean blood pressure was greatly reduced by bleeding, and electrocardiograms were recorded. The electrocardiogram did not show significant changes after the constriction (Fig. 6,*A* and *B*). Blood was then withdrawn until the mean blood pressure dropped to 10 mm. of mercury. After ten minutes, electrocardiographic changes developed. T_1 and T_2 became deeply inverted, and the RS-T segment in Lead V_3 became depressed (Fig. 6,*C*). These changes persisted for twenty minutes until the animal was transfused with the heparinized blood which had been previously withdrawn. Within five minutes T_1 returned to normal, the inversion of T_2 lessened, and the RS-T segment in Lead V_3 became isoelectric (Fig. 6,*D*).

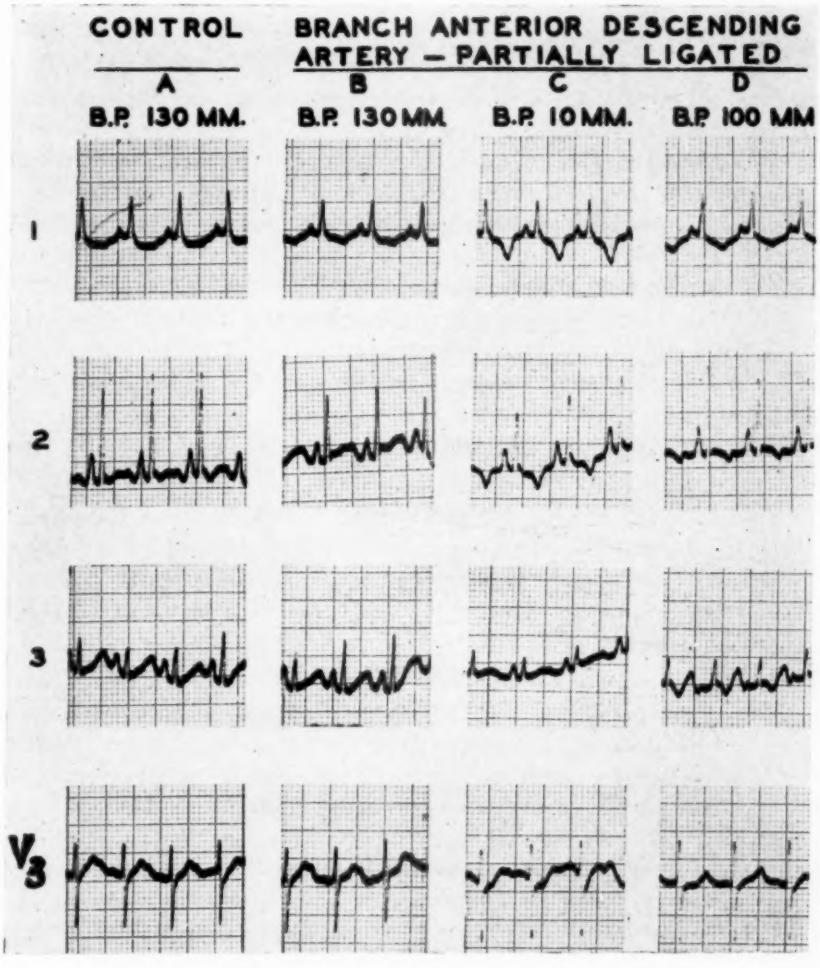


Fig. 6.—Electrocardiogram of dog.

A, Control electrocardiogram after pericardium was opened.

B, Electrocardiogram taken ten minutes after anterior descending coronary artery had been partially occluded. No significant change in the electrocardiogram.

C, Blood pressure now reduced by hemorrhagic shock. T_1 and T_2 are deeply inverted, T_3 is lower, and S-T segment in V_3 is depressed.

D, Blood pressure restored by transfusion. T_1 improved, T_2 less inverted, T_3 diphasic, and S-T segment in V_3 is isoelectric.

These changes are similar to those described by Master[17] as occurring in patients with coronary sclerosis who have sustained marked blood loss. They are due to the increased ischemia of the region supplied by the constricted artery resulting from the lowered blood pressure.

Experiment VII. Mechanism of the Lowered Blood Pressure After Coronary Occlusion.—

It is not the purpose of this paper to review the conflicting and inadequate evidence concerning the mechanism of shock which occurs after coronary occlusion in man. In at least forty dogs we have taken the blood pressure before, during, and after the ligation of large coronary arteries of the left ventricle. In some experiments we have ligated as many as eight major arteries of the left ventricle. In not a single dog, despite widespread loss of contractility, has there been a lowering of blood pressure for at least an hour or more after ligation of the arteries. If the mean blood pressure was low before the tie, as a result of hemorrhage and surgical shock, there was no further lowering after the artery or arteries were tied. The only time the blood pressure was reduced after a tie was when ventricular fibrillation supervened, in which case the blood pressure dropped rapidly to zero.

One may ask how these animal experiments differ from the dramatic shock-like state seen in patients after coronary artery occlusion.

In the dog, the pumping ability of the left ventricle does not appear to be impaired after coronary artery occlusion. Heart failure does not result since there is neither lowering of blood pressure, nor distention of the right ventricle, nor evidence of pulmonary edema. It would seem, then, that the shock state which occurs clinically is not directly due to heart failure.

It must be pointed out that the dog, the subject in these experiments, differs from man in several respects: (1) the dog is completely anesthetized; (2) the dog is completely atropinized; (3) in the dog, the remaining coronary arteries and myocardium are normal, whereas in human patients the nonobstructed coronary arteries may be the seat of advanced coronary sclerosis and there may be diffuse myocardial disease; and (4) of necessity the dog experiment is terminated in a few hours, whereas the patient may go into shock several days after the occlusion. The question of which of these reasons, if any, is responsible for the marked difference in behavior of the dog and man requires further study.

It is generally believed that shock with lowering of blood pressure and decrease in circulating blood volume is caused by one or two factors: (1) local fluid loss, and (2) visceral capillary atony.[18] After coronary artery occlusion in man, there is obviously no significant fluid loss into the ischemic region. It appears, therefore, that widespread capillary atony in both the general and pulmonary circulation is the most logical explanation for the development of shock. However, this capillary atony which may be the essential lesion in cardiac shock is difficult or impossible to demonstrate histologically.[19]

PART II. STUDIES ON THE TREATMENT OF SHOCK COMPLICATING CORONARY ARTERY DISEASE IN MAN

A. *Treatment of Shock in Acute Coronary Artery Occlusion.*—In view of our observations of the beneficial effect of treating experiment shock in the dog with coronary artery occlusion, we decided to apply vigorous treatment for the shock

of acute coronary occlusion in man. The treatment consisted of raising the blood pressure (1) by transfusion of whole blood or plasma or glucose solutions, and (2) by the administration of pressor drugs.

In simple uncomplicated cases without pulmonary edema we routinely administered intravenous plasma (treated with ultraviolet light to prevent hepatitis). Whole blood was used occasionally, especially in the presence of anemia. We feel that plasma is the fluid of choice because there is often hemoconcentration due to vomiting, diffuse sweating, and inanition. The use of saline or glucose parenterally seems less advisable because of the danger of pulmonary edema. If used, these solutions should be introduced slowly to prevent this complication. We used pressor amines, Neo-Synephrine, and epinephrine (1:1,000 solution), administering three to four minims of these substances every fifteen minutes. Caffeine and Coramine were also used. It should be clearly understood that these methods of treatment are experimental. The best method of treating shock after coronary artery occlusion is not known and is a practical problem worthy of extensive clinical and laboratory investigation.

It is of the greatest importance that while the patient is in shock the attending physician be in constant attendance to administer adequate but cautious treatment in raising the blood pressure and maintaining it at relatively normal levels.

If the patient had hypertension and cardiac hypertrophy previous to the occlusion, a systolic blood pressure of 110 or 120 mm. Hg after the occlusion may seem relatively normal. However, for that particular heart it is below the effective level and treatment should be instituted to raise it to approximately 150 mm. of mercury. If the blood pressure was normal before the occlusion, a systolic blood pressure of approximately 100 mm. Hg should be adequate. It should be recalled that the patient with acute coronary artery occlusion who is in shock is generally under profound sedation and the basal blood pressure of such patients is considerably less than when they are not under the influence of these drugs. For these reasons it is neither necessary nor advisable to raise the blood pressure to the patient's pre-existing normal blood pressure level.

The therapy should be instituted as soon as possible after shock develops. The longer the hypotension exists, the more coronary insufficiency and myocardial damage one can expect. Correction of severe hypotension after many hours or days of coronary insufficiency can be expected to produce myocardial failure, severe aneurysmal dilatation, or rupture of the heart. If the patient has been in shock for a long period of time, the prognosis is poorer and may be hopeless, because of irreversible changes. Myocardial rupture from the use of such therapy is unlikely if treatment is begun early, since rupture occurs from the tenth to twelfth day, by which time the patient is well out of shock.

Pulmonary edema is unfortunately a common occurrence after coronary artery occlusion and frequently occurs in patients with shock. Plasma or whole blood should be administered with caution, if at all, and the chief reliance must be placed on the pressor drugs. We have, however, not observed an accentuation of existing pulmonary edema in two cases in which plasma was administered.

The cause of pulmonary edema after coronary artery occlusion is not completely clear. The accepted explanation that it is due to left heart failure may be an oversimplification. In certain instances capillary atony, as it occurs in the toxemia of traumatic shock, may be an important element. The role of the central nervous system in the mechanism of pulmonary edema in patients is yet to be elucidated.[20]

We have treated many patients with shock by the methods which have been described, and in several instances the procedure has appeared to be life saving. Schwartz reported a similar case successfully treated.[21] Singer and Sampson[22] and Levine[23] have treated patients by transfusion with encouraging results. The following cases illustrate the usefulness of the treatment of shock after coronary artery occlusion. There have been failures, of course, but in no instance did the treatment appear deleterious.

CASE 1.—W. H. S., a 62-year-old man, was admitted to the hospital with dyspnea, profuse perspiration, and severe chest pain which had become progressively worse over a three-day period. His blood pressure at that time was 140/72. A diagnosis of myocardial infarction was made on the basis of electrocardiographic findings. He was put to bed and was given morphine for his pain and oxygen by nasal catheter. On the second day, the blood pressure was 125/90 and his pulse was rapid and thready. His breathing was still labored. The patient's condition gradually deteriorated and on the fourth day his blood pressure was unobtainable and his pulse rapid and irregular. The prognosis was considered grave.

He was given 1,000 c.c. of 5 per cent glucose in saline by intravenous infusion. Six hours later, his condition had improved remarkably, his pulse was regular, his blood pressure was 120/80, and he was no longer dyspneic. The patient's condition continued to improve in the next two days and his blood pressure remained above 118/78. A pericardial friction rub developed on the eleventh day, but the patient's subsequent course was uneventful and he fully recovered.

CASE 2.—S. H., a 54-year-old man, was admitted to the hospital in profound shock; he had complained previously of severe precordial pain. The patient's color was good, the skin was cold and moist, and the blood pressure could not be obtained. The patient was given 300 c.c. of plasma and 5 minims of epinephrine subcutaneously, and then was placed in an oxygen tent. Two hours later his blood pressure rose to 110/90 and his condition had improved somewhat, but he remained unconscious. An electrocardiogram revealed recent posterior myocardial infarction.

Blood pressure readings were made every hour. The morning of the second day his blood pressure was 90/70. In the next three-day period, the systolic blood pressure varied between 80 and 110 mm. of mercury. Whenever the blood pressure dropped below 90, as it did on five occasions in this period, 3 minims of epinephrine, 1:1,000, were administered. On the fourth day his condition again appeared to be very critical; he was in profound shock and his blood pressure remained below 90 mm. of mercury. He was given 300 c.c. of plasma and 1.0 c.c. of Coramine twice on that day. Following this, his blood pressure rose to 110 to 130 systolic, and his condition improved dramatically. On the fifth day he regained consciousness and for the next four days his condition was most satisfactory.

On the tenth day, however, the patient developed persistent paroxysmal auricular tachycardia. Despite all measures to break this arrhythmia, it continued for four days; the patient's condition deteriorated; and he died as a result of the arrhythmia.

CASE 3.—W. S., a 43-year-old man, was admitted to the hospital for treatment of hypertension. He complained of headaches and dizziness of two years' duration. Blood pressure on admission was 250/170 and the eye grounds revealed a Grade III retinopathy.

Left-sided sympathectomy was performed on July 14. After the operation the patient's blood pressure dropped to 120/90; the night of the operation there was further drop to 88/70.

The patient remained in a state of vascular collapse and at 4:30 P.M., July 15, he complained of severe precordial pain and his nail beds were cyanotic. At 7:15 P.M. he became markedly cyanotic and the electrocardiogram showed changes characteristic of a posterior myocardial infarction. At 11:00 P.M. the blood pressure had dropped to 60/40. The patient was unconscious and pale and his pulse was weak and thready. There appeared to be little hope of his surviving. At this time he was given a transfusion of 300 c.c. of plasma and within one hour the blood pressure rose to 118/80, at which level it remained all night. On the morning of July 16, he was again transfused with 300 c.c. of plasma and the blood pressure rose to 130/90. The patient's condition was markedly improved; cyanosis had disappeared, but he complained of precordial pain. Râles were present in both lung bases. The patient developed a pericardial friction rub on July 18. His blood pressure remained above 130/90 and his subsequent course and recovery were uneventful.

B. *Shock and Coronary Insufficiency.*—When shock of extracardiac origin occurs in patients with coronary sclerosis, electrocardiographic changes may develop.[17] After adequate transfusion, the electrocardiogram returns to normal.[23]

We demonstrated in Experiment VI that when shock occurs in a dog with a constricted coronary artery, the region supplied by that artery ceases to contract and balloons outward, becoming similar to the myocardium with complete arterial occlusion. In this experiment, electrocardiographic changes indicative of coronary insufficiency also occurred. When the blood pressure was restored in these animals by transfusion, the myocardial ballooning, cyanosis, and electrocardiographic changes disappeared. These observations and our knowledge of the mechanism of the collateral circulation of ischemic myocardium have led to a better understanding of so-called coronary insufficiency in man. The recent work of Blumgart,[24] Master,[25] and Levy[26] has contributed greatly to our knowledge of the subject. We have observed patients who developed electrocardiographic changes of severe coronary insufficiency after hypotension from surgical and hemorrhagic shock. The excellent therapeutic results of the treatment of shock in these cases appear to confirm our work on the effect of shock on the coronary circulation in dogs with partial coronary occlusion. It has been demonstrated repeatedly that patients and animals with very low blood pressure may develop electrocardiographic changes characteristic of myocardial insufficiency. This is especially true if there has been antecedent coronary artery disease, and is illustrated in the following cases:

CASE 4.—C. T., a 54-year-old man with known arteriosclerosis and moderate hypertension, was operated upon for the removal of a renal calculus. An electrocardiogram taken the day prior to surgery was normal. Spinal anesthesia was given. Afterward, the blood pressure gradually fell to 90/60. The anesthesia record showed the blood pressure remaining at this level for the duration of the surgery, approximately one and one-half hours. No pressor drugs were administered during this period. In anticipation of coronary insufficiency as a result of the prolonged lowered blood pressure, an electrocardiogram was taken immediately upon the patient's return to his bed. There was elevation of the RS-T segment with diphasic T waves in Lead V_2, and T_1 was flattened. The patient at this time was still under the effect of the morphine and anesthesia but was perspiring and had a rapid pulse.

Treatment by infusion of glucose in saline was cautiously administered and the systolic blood pressure soon rose to 150 mm. Hg, where it was maintained. The next morning another electrocardiogram was taken and the changes of the day before had disappeared entirely. The pattern was now similar to the original tracing. The patient made an uneventful recovery from his operation and there were no cardiovascular complications.

CASE 5.—J. M., a 62-year-old man, debarked from a plane with acute pulmonary edema after flying for many hours at high altitudes without oxygen. In previous years he had sustained two myocardial infarctions and was taking 0.2 mg. digitoxin daily. A few hours after the onset of pulmonary edema, his blood pressure dropped from 120 mm. to a level at which it could not be obtained. His skin was pale and cold and he perspired profusely. Dyspnea was marked and he was pulseless. His pulmonary edema improved with the shock state, but it was felt that he would surely expire. In view of the fact that he had such a poor coronary circulation, it was reasoned that his blood pressure should be raised or myocardial damage would result.

The patient was promptly given 5.0 mg. Neo-Synephrine and 2.0 c.c. Coramine intramuscularly and oxygen by mask. The blood pressure rose within a few minutes, but on several occasions the systolic pressure dropped below 95 mm. of mercury. By means of repeated injections of epinephrine and Coramine, the blood pressure was sustained for two hours and then it remained above 110 mm. of mercury. His condition improved gradually until it appeared that he would survive. His pulmonary edema did not recur and his subsequent recovery was dramatic.

DISCUSSION

It was shown in these experiments that the coronary circulation of animals with coronary occlusion and reduced blood pressure differs in two important respects from that of animals with coronary occlusion and normal blood pressure: (1) there is a significant reduction in the collateral blood supply to ischemic portions of myocardium, and (2) there is a significant reduction in the blood supply to other (control) parts of the myocardium. These observations were made in both the radioactive red blood cell experiments and the fluorescein experiments.

Decreased Circulation to the Ischemic Myocardium.—In the animals with reduced blood pressure the decreased circulation to the ischemic region is obviously due to the reduced pressure gradient. The pressure in all the vessels of the ischemic region is very low in both normotensive and hypotensive animals. But in normotensive animals the pressure in the accessory coronary arteries is high enough to force abundant blood into the ischemic region in a relatively short time. In hypotensive animals, however, the pressure in the nonobstructed coronary arteries is also low and the collateral blood flow into the ischemic region is greatly reduced.

Since the collateral blood supply to the ischemic region nourishes the ischemic myocardium, promotes healing, and reduces the size of the infarct, decreased filling such as occurs in shock would be expected to have a deleterious effect upon ischemic myocardium. One would therefore expect the incidence of cardiac rupture to be greater in patients who have been in shock for some time, since under this circumstance necrosis and myocardial weakening could have progressed. In addition, the incidence of aneurysmal dilatation of the ischemic region in the left ventricle may be less in patients in whom shock had not been present.

Decreased Circulation in Nonischemic Myocardium.—The observation that with low blood pressure there is a reduced circulation in regions of myocardium supplied by nonoccluded arteries is probably even more significant than the observation of diminished collateral blood flow to the ischemic myocardium. This was found in both the radioactive red blood cell and fluorescein experiments.

It should be pointed out that the nonobstructed coronary arteries in the dog are normal, whereas in patients with coronary disease there is usually present more or less occlusive vascular changes in the nonobstructed arteries. Therefore, the effect of hypotension on the so-called nonischemic portions of the left ventricle in patients with coronary occlusion is more marked (with more significant reductions in blood flow) than in dogs with an equivalent reduction in blood pressure. Thus, in patients with shock, not only does the region supplied by the occluded vessel have a diminished blood flow, but there are probably significant degrees of ischemia in large segments of myocardium, the major arteries of which are not completely occluded. This could also account for the myocardial necrosis found in nonischemic regions in patients in shock, described by Blumgart,[24] and the subendocardial necrosis more recently described by Master and his coworkers.[17] The finding that the blood flow to nonischemic regions of the left ventricle is reduced offers an explanation for the myocardial insufficiency referred to earlier.[1-7]

It has been claimed by others that coronary insufficiency does not occur during the hypotension following shock. The reason given is that the work of the heart is reduced in proportion to the reduction of coronary blood flow. This concept is not substantiated by our experiments on shock in both animals and human subjects. In dogs, increased ballooning and increased cyanosis were seen as a result of the shock state. In man, electrocardiographic changes indicative of coronary insufficiency were observed with shock. If the reduced work of the heart were actually a means of compensating for coronary insufficiency, these signs would not appear.

Myocardial Contractility and Shock.—In both man and the experimental animal it has been demonstrated that the region of myocardium supplied by an occluded artery may become noncontractile. Detailed studies of noncontractility in ischemic myocardium have been made in this laboratory.[16] Although the mechanism of noncontractility is not known, it was shown that it is related to, and occurs as a result of, ischemia and anoxia. In the present study it was shown that in dogs with partial occlusion of the coronary arteries, contractility of the involved myocardium remained normal. When the blood pressure was reduced, the region supplied by the constricted vessel ceased to contract and ballooned markedly. This observation is of the greatest clinical importance, since patients who have myocardial infarctions from coronary artery occlusion usually have generalized coronary sclerosis and narrowing of other coronary vessels. Thus, as in the experimental animal, the reduction of blood pressure resulting from a coronary artery occlusion in man probably results in noncontractile regions of myocardium where there is coronary sclerosis but no occlusion. As shock becomes more intense in such cases, the noncontractile region should become more extensive. This sequence of events would exert a severe strain upon the remaining contractile portion of the left ventricular myocardium, particularly as the nourishment to this portion is also reduced. The persistence of this situation must result in death, and its occurrence may well serve to explain the fact that the mortality after coronary artery occlusion is increased if shock is a complicating factor. Whether the terminal arrhythmia is ventricular fibrillation or

ventricular asystole, as a result of the grossly altered mechanics, is of minor importance. Unless efforts are made to correct the fundamental defect, it seems useless to administer a drug such as quinidine in an attempt to prevent ventricular fibrillation in a heart with large noncontractile regions and with only a small portion of ischemic left ventricle contracting.

From the experimental evidence that has been obtained in this study, it would seem that as long as the blood pressure remains normal there is apparently normal coronary blood flow, with resulting normal myocardial contractility and absence of both cyanosis and electrocardiographic changes. This may be the result of vasodilatation of the vessels in the involved region, which maintains the normal blood flow despite a marked reduction in the lumen of a coronary artery and a reduced pressure gradient distal to the stenosis. It is also possible that the blood flow to the potentially ischemic region is enhanced by the intercoronary arterial anastomoses because the pressure in these anastomoses which are supplied by nonobstructed arteries is higher than the pressure in the constricted artery. Possibly the persistence of this pressure gradient in the interarterial anastomoses and the increased blood flow through them constitute a stimulus for their gradual enlargement.

In view of the widespread existence of coronary sclerosis in a large proportion of adults in the fifth to seventh decades, the significance of this observation cannot be overemphasized. As long as the blood pressure remains normal, the blood flow to the potentially ischemic region may remain normal because of vasodilatation and the gradual enlargement of the existing intercoronary anastomoses which are of great value when the closure finally becomes complete. The intercoronary anastomoses which become prominent during the many years of partial ischemia may well save the patient's life. As Blumgart[27] has shown, these intercoronary anastomoses may be large enough to prevent tissue necrosis, so that the final closure may be completely silent and unaccompanied by clinical signs or electrocardiographic changes.

If the blood pressure is reduced, the region of myocardium supplied by the constricted artery loses its ability to contract and becomes cyanotic. Electrocardiographic changes indicative of myocardial ischemia occur under these circumstances. Since stenosed arteriosclerotic coronary vessels are more frequently observed in individuals in the older age groups, it is particularly important to prevent and treat the shock and low blood pressure which may result from surgical operations, anesthesia, accidents, hemorrhage, infections, intoxications, burns. Such older patients die not only from the direct effects of shock but from irreparable secondary damage to the heart. In the experimental animal the heart improves rapidly when the blood pressure is elevated; the ballooning disappears and the electrocardiographic changes regress or disappear. Careful observation of the heart in magnified, slow-motion pictures taken soon after the elevation of the blood pressure shows that it is transformed from a malfunctioning, cyanotic organ into a mechanically efficient and apparently normal organ.

Treatment of Shock.—It is obvious that in many patients in shock, with coronary occlusion, the organic damage to the heart is so severe that death is

inevitable, regardless of the treatment. Likewise, there are undoubtedly some patients with relatively mild shock who recover without any specific treatment of the shock. Between these two extremes there is a variable number of cases in which the treatment of the shock may be a life-saving procedure. Although the final purpose is to restore the blood pressure and thereby improve the coronary circulation, the best method of achieving this aim is still to be worked out. Enough is known, however, to allow the physician to do all that he can by methods available to everyone to elevate the blood pressure and thus preserve the myocardium.

The treatment of shock after coronary artery occlusion now appears to rest on a firmer clinical basis. From the experiments done under controlled conditions in experimental animals, there is strong indication for vigorous and intelligent treatment which may indeed be spectacular. Since the mechanism of the shock which follows coronary artery occlusion is unknown, the most desirable treatment to raise the blood pressure is more or less empirical at the present time. In our experience, the use of plasma and blood and the careful use of the pressor amines have appeared to be life saving in a few selected cases. Since shock does not occur in the animal with experimental coronary artery occlusion, the problem can be answered only by means of carefully controlled clinical studies which, we hope, will more clearly define the exact therapeutic procedure indicated in any particular case.

It has been thought that the work of the heart is reduced as a result of the decreased blood pressure and that the low blood pressure should not be treated.[8,9,10] But in patients with antecedent diffuse coronary disease and with hypertrophied left ventricles, the coronary flow may be suboptimal with preexisting blood pressure levels. Lowering of the blood pressure in such patients, although it may reduce the work of the heart, seems to cause an increased myocardial insufficiency, and actual tissue necrosis has been observed histologically in such cases.

Heart failure rarely occurs in dogs after experimental coronary occlusion, but it frequently occurs after coronary artery occlusion in man. The myocardial insufficiency in dogs is probably insignificant because the nonobstructed coronary arteries are normal. In man, however, the generalized coronary artery disease probably results in more generalized myocardial ischemia during hypotension, and this may explain the heart failure which sometimes follows small or moderately large myocardial infarctions.

The danger that myocardial rupture may result from the early use of therapy to raise the blood pressure is probably overemphasized, because rupture generally occurs only on about the tenth to fourteenth day after coronary occlusion.[28] Raising the pressure at this time could easily cause rupture of the myocardium, because tissue necrosis has already occurred. It is possible that the early elevation of the blood pressure would prevent tissue necrosis and allow for better healing of the ischemic regions, thereby preventing the myocardial necrosis which is the cause of ventricular rupture.

Coronary occlusion is common in patients with hypertension. In such cases the blood pressure may fall markedly and be insufficient for the hypertensive

patient with cardiac hypertrophy, despite the fact that the blood pressure does not fall below levels considered to be normal in the normotensive patient. Patients with markedly hypertrophied left ventricles caused by hypertension, who have a so-called normal blood pressure after coronary occlusion, should be treated as though they were in shock. Hypertensive patients without marked left ventricular hypertrophy may be treated more conservatively. Sedation alone causes reduction in the blood pressure of hypertensive individuals. Therefore, it should be emphasized that the therapy that is being recommended applies to patients with pronounced lowering of the blood pressure and that such therapy must be administered with caution. For instance, if the systolic blood pressure before coronary occlusion had been maintained around the level of 220 and it dropped to 110 mm. Hg after occlusion, it should probably be raised to about 150 mm. Hg, if possible.

In unpublished observations from this laboratory, it was found that the rate of absorption of subcutaneously administered materials can be quantitatively and simply determined by means of radioactive isotopes. It was found, in experimental animals, that the absorption was greatly delayed after hemorrhage and improved after transfusion. There are clinical applications of these experimental observations. Occasional patients in shock, after coronary occlusion, still have severe substernal pain. The usual rule is that these patients receive ¼ grain morphine sulfate every fifteen minutes subcutaneously. This procedure may be illogical, for two reasons. The patient may receive little relief, since only a small fraction of the drug may be absorbed from the site of local injection. This may result in repeated injections for the production of an effect. Then, if the blood pressure should become elevated spontaneously or as a result of specific treatment, the large unabsorbed depot of morphine may be rapidly absorbed and death may result from an overdose of morphine.

Our knowledge of the mechanism of traumatic and surgical shock is much more advanced than our knowledge of shock after coronary occlusion. Furthermore, it is known that shock is not a distinct entity and may result from a variety of causes which require different treatment. It is possible that the shock which follows coronary occlusion also results from a variety of causes. Such causes may include (1) reflex influences, (2) mechanical factors, or disturbed dynamics, (3) toxic effects, as from myocardial necrosis, or (4) combinations of these factors. Boyer[30] has thoroughly reviewed the subject of cardiogenic shock. As a result of extensive experimental investigation on shock from wounds, burns, infection, and certain types of intoxication,[7,18,19,29] we feel that the factor of capillary atony should be carefully considered. Obviously there are many types of shock, and after coronary artery occlusion more than one factor may be responsible for the capillary atony which may well explain the hypotension.

The ideal treatment in any individual case should depend upon the cause, and until further knowledge is obtained on the factor or factors causing shock, after coronary occlusion, the treatment must remain largely empirical. Regardless of the mechanism of the shock, however, the results of our experiments show that it is of great importance promptly to overcome extreme hypotension which is associated with coronary occlusion or which occurs in coronary insufficiency.

CONCLUSIONS

1. A series of experiments has been performed to study the effect of shock, with or without coronary artery occlusion, on the coronary circulation and on myocardial contractility.

2. The first method consisted of the intravenous injection of radioactive erythrocytes into dogs with ligated coronary arteries and marked reduction of blood pressure induced by hemorrhage.

3. It was found that with low blood pressure levels the coronary blood supply in nonobstructed vessels was greatly reduced, as was that through the collateral intercoronary anastomoses.

4. In slow-motion pictures of the heart, special lighting allowed intravenously injected fluorescein to become visible after it reached the coronary arteries. In confirmation of the observations made with the radioactive red blood cells, this method also showed that the coronary circulation is greatly diminished in shock. With reduced pressure gradient through interarterial anastomoses, the blood supply to regions made ischemic by ligation of coronary arteries was much less than in animals with normal blood pressure.

5. After coronary artery ligation, the region supplied by the ligated artery usually lost its contractility and ballooned outward during systole. With the production of shock, the region of noncontractility became much more extensive and the ischemic region became more cyanotic. Electrocardiographic changes indicative of myocardial ischemia occurred.

6. After transfusion of heparinized blood, contractility of the ischemic region improved, cyanosis decreased, and electrocardiographic abnormalities regressed or disappeared. This was the result of the improved nutrition via the collateral circulation to the region normally supplied by the ligated artery.

7. Constriction of the lumen of the coronary arteries, simulating coronary sclerosis, affected neither contraction nor color of the potentially ischemic region while the blood pressure was normal. The coronary blood flow appeared to be normal according to the inflow of fluorescein in this region. The normal blood flow resulted from vasodilatation in the potentially ischemic region and the increased flow through interarterial anastomoses maintained by the intercoronary pressure gradient. These observations explain normal myocardial function in the older age group with coronary sclerosis.

8. If the blood pressure was lowered in animals with partial coronary ligation, contractility was diminished or absent and the entire heart, especially the ischemic region, became cyanotic. After blood transfusion and restoration of normal blood pressure, normal contractility returned and cyanosis disappeared.

9. These observations on coronary blood flow and noncontractility explain on a physiologic basis "coronary insufficiency" or "coronary failure." Our observations offer good physiologic reasons for correcting shock and low blood pressure due to various causes in the older age groups.

10. The mechanism of clinical shock following coronary artery occlusion is unknown. In dogs, there is no lowering of blood pressure, evidence of left heart failure, or pulmonary edema following extensive ligations of many of the coronary arterial branches of the left ventricle.

11. As a result of the experimental observations in patients with shock after coronary artery occlusion, one may reasonably believe that there exist regions of noncontractility in the myocardium. If noncontractility becomes sufficiently extensive, death is inevitable. In this state of shock, a small functioning segment of the myocardium of the left ventricle has a greatly reduced blood supply, yet is called upon to do the work of the entire left ventricle.

12. The low blood pressure of shock, after coronary artery occlusion, must be vigorously, intelligently, and immediately treated. In a few cases, it was demonstrated that intravenous plasma, whole blood, and the judicious use of pressor drugs may prove to be life saving.

The authors desire to thank Dr. S. L. Gabby and Dr. J. Sugarman for allowing us to present Cases I and III, Mr. S. A. Sanford and Mr. John Bishop for their excellent work in motion picture photography, and Mr. Irving Paris for technical aid in the isotope experiment.

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THE ELECTROCARDIOGRAPHIC DIAGNOSIS OF THE DISTURBANCES OF THE HEART'S VENOUS CIRCULATION

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THE construction and function of the venous system of the heart are still not known in all their details. According to our present knowledge, the blood which reaches the heart through the arterial system leaves the myocardium in five different ways: (1) through the capillaries into the veins of the heart and thence through the coronary sinus into the right atrium; (2) through the capillaries into the Thebesian veins and thence into the ventricular cavity; (3) through the so-called luminal arteries directly into the ventricle; (4) from the so-called sinusoid arteries through the myocardial sinuses into the ventricular cavity; and (5) through extracardiac anastomoses, and thence indirectly into the main venous system of the body.

In case the coronary arterial blood is interfered with in its return to the heart, venous congestion occurs. The question to be considered is whether congestion of the myocardium, resulting from disturbance of the venous circulation, produces anatomic or functional changes in the heart muscle, and if so, whether this is revealed by the electrocardiogram.

Laufer,[6] after tying the coronary sinus, did not observe any change in the ventricular muscle, but did observe some degree of fibrosis in the atrial muscle. The animals used in these experiments withstood the obstruction of the sinus very well. These experiments seemed to support Condorelli's[3] opinion that venous congestion of cardiac muscle only injures the atrial muscle. From the electrocardiographic point of view, the problem was studied by several workers[1,4,8] who found that obstruction of the coronary sinus produced either no change or only a moderate change in the size or direction of the T wave.

I did not think it likelythat venous congestion could exist without causing some characteristic electrocardiographic change. I based my opinion on two considerations: one was the fact that the electrocardiogram is extremely sensitive to disturbances of the arterial circulation to the heart. It did not seem probable that disturbance of the venous circulation could be present without exercising any effect. The other fact was the capacity of the heart's venous circulation; it would seem to be so abundant in order to insure against the possibility of the

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Editor's Note.—The experimental observations reported in this paper were to have been presented at a Plenary Session of the Third Inter-American Cardiological Congress, Chicago, Ill., June 13-17, 1948. Unfortunately, the author found it impossible to attend the Congress.

development of venous congestion. I could not believe, therefor, that if disturbance of the venous circulation develops this would not injure the ventricular muscle and affect the electrocardiogram. My conviction was proved by the results of experiments on animals.

EXPERIMENTAL METHOD AND RESULTS

In order to produce venous congestion, I partially or completely obstructed the coronary sinus, since it seemed likely that this procedure would produce disturbance of venous circulation in the whole heart.

The technical part of the experiment consisted of partially or entirely tying off the coronary sinus of a dog's heart almost immediately before its entrance into the right atrium. After tying off the sinus I observed the heart muscle for one hour or more and recorded electrocardiograms (three standard limb leads and Lead CF_4) every five minutes.

Within a few minutes after tying off the coronary sinus one could observe the ventricular muscle becoming somewhat cyanotic; it maintained this shade through the whole experiment. Shortly after removal of the ligature from the coronary sinus, the heart muscle recovered its natural color.

An essential change was observable in the serial electrocardiograms. In all three limb leads and in the chest lead as well, the amplitude of the QRS complex slowly and gradually decreased. The maximum reduction in voltage developed ten to thirty minutes after the obstruction. The variation in the time of development of the maximum change most likely depended upon whether the coronary sinus was obstructed entirely or only partially. In any event, as a consequence of venous congestion of the myocardium, low-voltage QRS complexes developed in the electrocardiogram.

Two types of low-voltage complexes could be distinguished. In the type which I call the *R Type*, the R wave becomes smaller (Fig. 1). In the other type, which I call the *S Type*, in addition to the R wave becoming smaller, a more or less deep S wave appears (Fig. 2).

Except for the development of low voltage of the QRS complex, the electrocardiogram is not greatly affected. The P wave is not essentially changed, though it usually becomes somewhat higher in the three limb leads. The RS-T segment remains on the isoelectric line during venous congestion. In some cases the T wave shows no change, but in most cases this wave becomes lower or even inverted.

After removal of the ligature from the coronary sinus which thus relieves the venous congestion, all electrocardiogram deviations usually disappear within ten to twenty minutes.

DISCUSSION

As the result of my animal experiments, I have concluded that venous congestion of the myocardium which results from the tying off of the coronary sinus harms the heart muscle as a whole. This is shown not only by the development of low-voltage QRS complexes but also by the pathologic changes which the

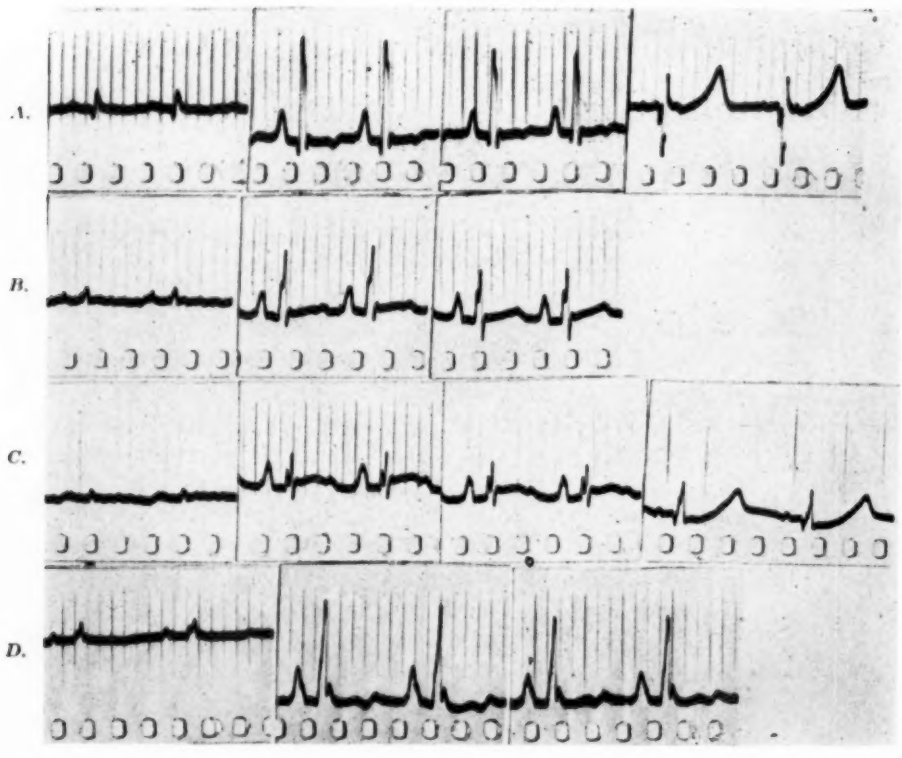

Fig. 1.—*A*, Leads I, II, and III and a lead similar to Lead CF_4 in a dog. *B*, The electrocardiogram made ten minutes after the tying off of the coronary sinus. *C*, Electrocardiogram made twenty minutes after the tying off of the coronary sinus. *D*, Electrocardiogram made ten minutes after removal of the ligature from the coronary sinus.

The tracings clearly show that obstruction of the coronary sinus causes the QRS complex to become smaller in the limb and chest leads. Since the low voltage results from lowering of the height of the R wave, this is the *R Type* of *pathologic low voltage*. (See text.)

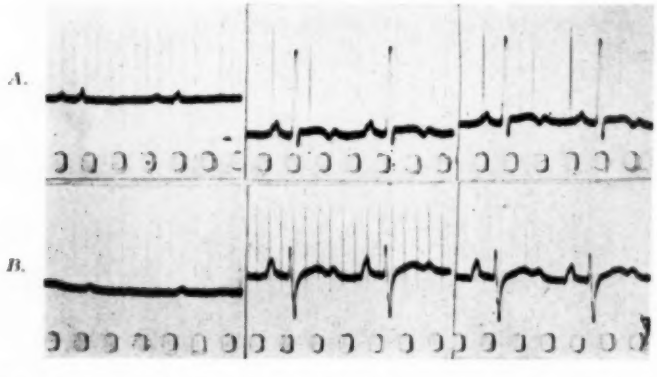

Fig. 2.—*A*, Leads I, II, and III of a dog. *B*, Electrocardiogram made thirty minutes after the tying off of the coronary sinus.

The figure clearly shows that the QRS complex becomes smaller as the result of the tying off of the coronary sinus. This is an example of the *S Type* of *pathologic low voltage;* the R wave becomes lower and an S wave becomes larger. (See text.)

T wave undergoes. On the basis of my experiments I feel justified in stating that the pathologic low-voltage electrocardiogram is just as characteristic of disturbance of the venous circulation of the heart as is the electrocardiogram with typical patterns for obstruction of the arterial circulation.

I do not wish to discuss further the implications of these experimental results at this time. In another article I shall attempt to deal with other phases of the subject, including the application of the results of my experiments to human pathology, including myocardial infarction, mitral stenosis, and other lesions.

SUMMARY AND CONCLUSIONS

1. Venous congestion injures the ventricular muscle.

2. As a result of the injury produced by venous congestion, pathologic electrocardiographic changes develop.

3. In these abnormal electrocardiograms, low-voltage and pathological changes of the T wave are striking and consistent. For this reason I have called the pattern, "pathological low-voltage."

4. With the disappearance of venous congestion, the pathologic electrocardiogram, and therefore the abnormal state of the ventricular muscle, return to normal within a short time.

5. I consider that the pathological low-voltage pattern is just as characteristic of venous congestion of the myocardium as the electrocardiogram with certain typical findings is characteristic of obstruction of the arterial circulation.

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THE GRAPHIC REGISTRATION OF BASAL DIASTOLIC MURMURS

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THE high-pitched blowing diastolic murmur heard most characteristically in slight aortic regurgitation is at times extremely faint, and the most careful auscultatory technique is necessary for its detection. The decision as to the presence or absence of such a murmur is of the greatest importance, for clinical experience has indicated that the diagnosis of aortic insufficiency is unwise unless the presence of the murmur can be established without a doubt. The usual auscultatory technique cannot be depended upon when the loudness of the murmur borders on the average threshold of human hearing, and as a result, differences of opinion arise even among the most competent clinicians.

The development and commercialization of the modern electronic phonocardiograph led to its application to the detection of faint aortic diastolic murmurs with the hope that instrumentation would provide a more positive method for their detection. However, it was found that the usual commercial phonocardiograph was unsuitable, in that it often failed to register the faint, high-pitched murmur although its presence was well established by auscultation.[1,2] On the other hand, it was observed that low-pitched sounds and murmurs, such as the auricular sound, the third sound, and the mitral diastolic murmur, all of which lie at the opposite extreme of the auscultatory spectrum, were registered distinctly even though they were at times inaudible.[3,4,5] The impression was thus created that faint, high-pitched murmurs cannot be registered phonocardiographically, although they are audible on careful auscultation with the acoustic stethoscope. As a result of this concept, there has been no satisfactory study by phonocardiography of the basal diastolic murmurs.

Our observations indicate that failure to register the faint, high-pitched basal murmurs has been caused by several factors. The first of these is that the phonocardiograph may have insufficiently high sensitivity and insufficiently high deflection speed to record these murmurs. Second, the instrument may not provide sufficient attenuation of the lower frequency vibrations in comparison with the vibrations of higher frequency. If this is the case, it is impossible to use sufficient amplification to register the higher frequencies because the lower frequency vibrations will then have such a large amplitude as to make satisfactory recording and analysis of the tracing impos-

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sible. Third, the physical and physiological factors that are involved in the production of such murmurs may not be properly understood. Finally, failure to register these murmurs may be due to an imperfect phonocardiographic technique.

It is of greatest importance in phonocardiography that the response of the instrument used with respect to the different frequencies be both understood and clearly stated. This means that the accentuation or attenuation of the intensity of vibrations with regard to their frequency should be placed on record. It is only in this manner that tracings taken with different instruments can be interrelated. A study of heart sounds and murmurs by means of calibrated phonocardiography has recently been made by Mannheimer.[6] He has used six channels, recording vibrations in six separate, but overlapping, frequency bands. Each of these channels has a linear response, which means that the intensity of the vibrations is not accentuated or attenuated with regard to their frequency. It is interesting to observe the considerable difference in the configuration of the sounds and murmurs, even in adjacent frequency bands. Indeed, some murmurs recorded in one band cannot be identified in the adjacent band. This marked difference illustrates the danger of drawing any conclusion about the configuration of sounds and murmurs, or even about their presence or absence, from tracings taken with phonocardiographs in which the frequency response is not known. The calibrated phonocardiograph fulfills the requisites of proper statement and description of frequency response characteristics and is a useful instrument for harmonic analysis. It is difficult, nevertheless, to correlate the tracings with what is heard on auscultation.

The phonocardiograph most satisfactory for correlation with auscultatory findings is an instrument in which the various frequencies of the auscultatory spectrum undergo the same modification with regard to intensity as occurs with the average acoustic stethoscope, together with that of the average human hearing mechanism. In this way the graphic representation most approximately parallels the auditory impressions obtained on auscultation. In addition to a frequency response of this character, it is desirable to be able to use an alternative frequency response in which there is less relative attenuation of the lower frequencies. This will enable the registration of the lower frequency components of audible and subaudible sounds and murmurs. We have therefore used in this study the Sanborn Tribeam phonocardiograph, with stethoscopic and logarithmic microphones and interchangeable chestpieces.[3,4]

The purpose of this paper is to analyze the physiological and physical factors which are involved in the production of the basal diastolic murmurs, to present a phonocardiographic technique which has proved satisfactory in their reproduction, and to describe the graphic configuration of these murmurs. We have included in this study murmurs due to aortic and pulmonary regurgitation, together with a discussion of tracings showing diastolic vibrations where no murmur was heard. Patients with continuous murmurs from patent ductus arteriosus, arteriovenous aneurysm, and venous hum have been excluded.

PHYSIOLOGICAL AND PHYSICAL CONSIDERATIONS

The murmurs of aortic and pulmonary regurgitation result from the backflow of blood from the great vessels into the heart during the diastolic phase of the cardiac cycle. This is usually due to deformity of the value cusps which may vary in extent, even to retroversion or perforation of the cusps. It may be due, however, simply to a dilatation of the aortic or pulmonary ring and under these circumstances be reversible. Occasionally regurgitation may commence with the occurrence of vegetations on a valve that previously functioned normally, as has been found in the congenital bicuspid aortic valve.[7] There are several factors which determine the character of the murmur, the first of these being the size of the opening through which regurgitation is taking place. Clinical experience has shown that when free aortic regurgitation increases in severity there may be a reduction in the intensity of the murmur. The second factor is the difference in pressure on either side of the opening. From an analysis of the pressure curves obtained by Wiggers[8] in normal animals and in those with aortic regurgitation, it can be seen that the difference in pressure on either side of the aortic valve increases from the time of its closure until just after the time of opening of the auriculoventricular valves. The maximal difference of pressure is between 0.08 and 0.10 second after the closure of the semilunar valves, and this is followed by a slowly declining pressure difference. A third factor is probably the size of the cavity into which regurgitation is taking place. Finally, it may be that the turbulence produced by the closure of the semilunar valves is such as to keep even deformed cusps in temporary apposition and thus momentarily to delay the onset of regurgitation. The last three factors may help to explain the configuration of the murmurs illustrated in this paper.

AUSCULTATORY CHARACTERISTICS OF THE BASAL DIASTOLIC MURMUR

The usual descriptions of the murmur state that it either replaces or follows immediately the second heart sound. It may be either high or low pitched and usually is of a blowing character and diminuendo throughout its duration. Only one[9] of the widely used textbooks states that there may be some delay between the end of the second sound and the onset of the murmur. None of them mentions that the murmur may ever be other than decrescendo in character. However, we have found on careful auscultation that the murmur has sometimes an early crescendo phase before the longer decrescendo phase, and Dr. Paul D. White personally stated[10] that he has not infrequently heard basal diastolic murmurs of this character. Those workers who have described the phonocardiogram in patients with aortic or pulmonary regurgitation have not shown this pattern.[11,12] Nevertheless, we shall demonstrate that a crescendo-decrescendo configuration is found on tracings not only from those patients in whom this is noted on auscultation, but also quite frequently from patients in whom the murmur is heard as purely decrescendo in character.

PHONOCARDIOGRAPHIC TECHNIQUE

The technique of taking sound tracings is of considerable importance. The patient should be comfortable and warm, and in a quiet room free from nearby sources of interference from alternating current. The sound or murmur to be recorded should be carefully located and the point of maximal intensity determined. The stethoscopic microphone and audiophone are then used to confirm the similarity of the electrical reproduction to what was heard with the acoustic stethoscope, and a choice of chestpiece best suited to register the murmur is made.

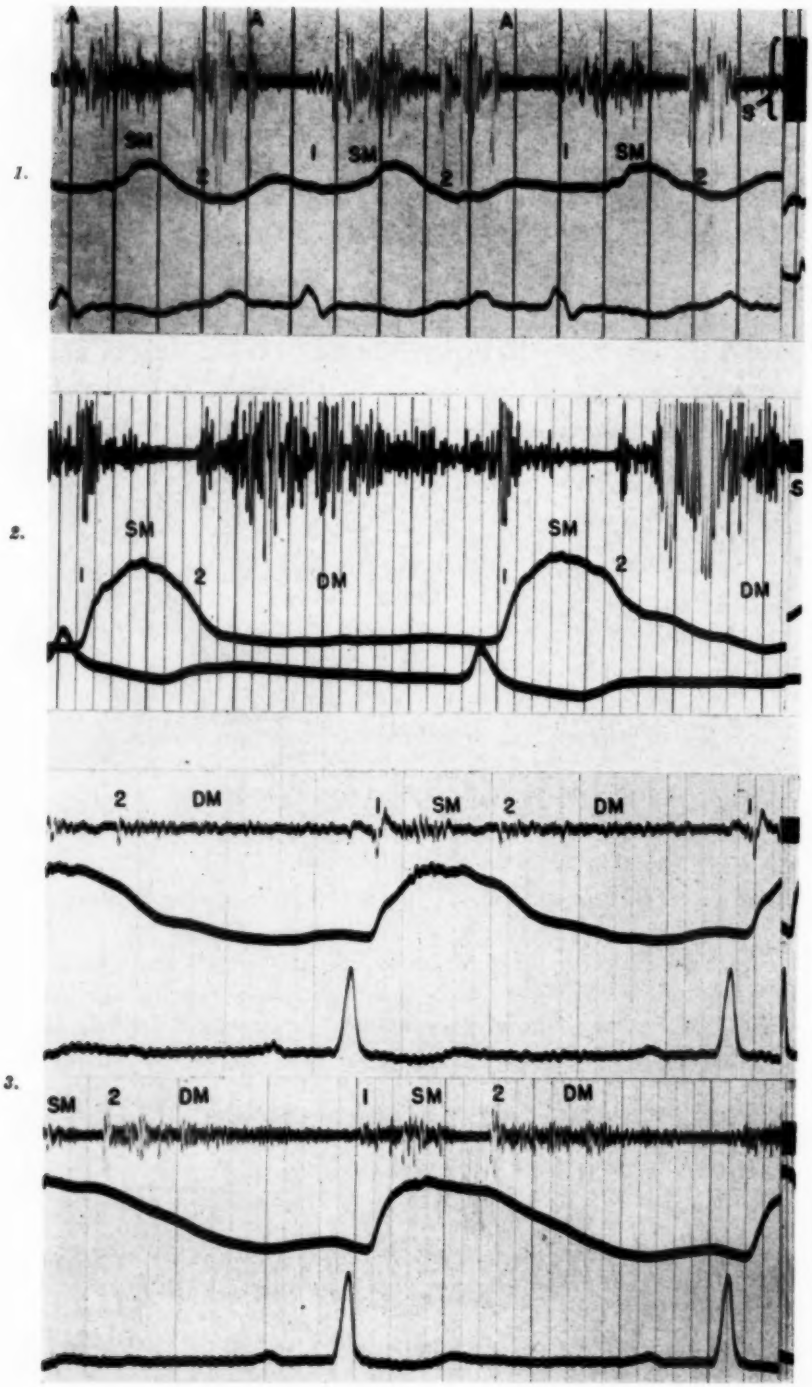
The most useful chestpiece for the high-pitched type of diastolic murmur is the Bowles chestpiece with Bakelite diaphragm 0.015 inch thick and with a free working diameter of 1-3/8 inches. These are the diameter and thickness most commonly used in the commercial acoustic stethoscope. The Bowles chestpiece is used only with the logarithmic microphone. When the murmur is extremely high pitched and faint, a similar Bowles chestpiece with a Bakelite diaphragm of 0.035 inch thickness is occasionally more satisfactory.[3] However, in the majority of tracings taken in this study, we have used the open bell chestpiece with the logarithmic microphone. This combination is somewhat more satisfactory when the murmur to be reproduced is of moderate or low frequency.

The application of the chestpiece must be made with care so that it is perfectly sealed to the chest wall. When the cardiac impulse is forceful, or during certain phases of respiration, there may be temporary lifting of the chestpiece from the chest wall. This produces artefacts on the tracing of which the operator may not be aware at the time the tracing is taken, especially when proper correlation with the auscultatory findings has not been made. Fig. 1 shows a tracing in which such artefacts are present.

The position of the patient should be altered by means of an easily adjustable couch or bed until the jugular pulse in the neck is most clearly seen. The sound tracings are taken in this position, so that satisfactory jugular pulse tracings can be made at the same time. In an occasional case in which the murmur is audible only in some other position, further tracings can be taken subsequently in the desired position. All records are taken with the breath held in expiration.

The degree of amplification must be determined by experience. We have not considered it necessary to keep the upper parts of loud sounds and murmurs on the 6.0 cm. paper. With insufficient amplification the tracings must be studied by means of a magnifying glass and are unsuitable for analysis or reproduction.

We have recently standardized our phonocardiograms by means of a sound source of constant frequency and intensity, namely, 500 cycles a second at 80 decibels above the threshold of audibility. After each tracing is made and before the controls of the instrument are touched, the microphone is removed from the patient, the chestpiece is detached, and the standard sound is introduced. The width of the dark band at the end of the tracings therefore represents a



Figs. 1-3.—*See opposite page for legends.*

constant reference of sound intensity analogous to the one millivolt used in the standardization of the electrocardiogram. A full description of this standardization is the subject of a separate communication.[13]

All of our tracings have been taken at a paper speed of 75 mm. per second.

When carefully attentive to technique, we have never failed to record even the most faint diastolic murmur and have frequently demonstrated murmurs where auscultation had produced a difference of opinion as to their presence. In addition, there have been cases in which no diastolic murmur was ever heard but in which we have registered vibrations in early diastole. Tracings of these patients will be shown, and the reasons why such vibrations were not audible will be discussed.

LOUD BASAL DIASTOLIC MURMURS

The intensity of murmurs as they are heard on auscultation may be usefully expressed in the manner introduced by Levine.[14] A murmur is considered to be Grade 6 in intensity when it can be heard with the ear at some distance from the chest wall, while very loud, moderate, slight, and very slight murmurs are classified as Grade 5, Grade 4, Grade 3, Grade 2, and Grade 1, respectively. The loud (Grade 4) basal diastolic murmurs are very easily recorded, and it is in these murmurs that a crescendo-decrescendo configuration can most readily be demonstrated. The first tracing (Fig. 2) is taken from a patient in whom the character of the murmur on auscultation was such that it increased in intensity in early diastole, then gradually diminished in intensity up to the time of the subsequent first heart sound. The tracing shows that the maximal intensity of the murmur occurs between 0.10 and 0.20 second from the closure of the semilunar valves.

The patient whose tracing is shown in Fig. 3 had on auscultation a murmur of more usual character. It was loud and blowing and was thought to be purely decrescendo. The stethoscopic tracing demonstrates how poorly this microphone reproduces the murmur, while in contrast, the low frequency components of the first sound and the systolic murmur are well recorded. This is because

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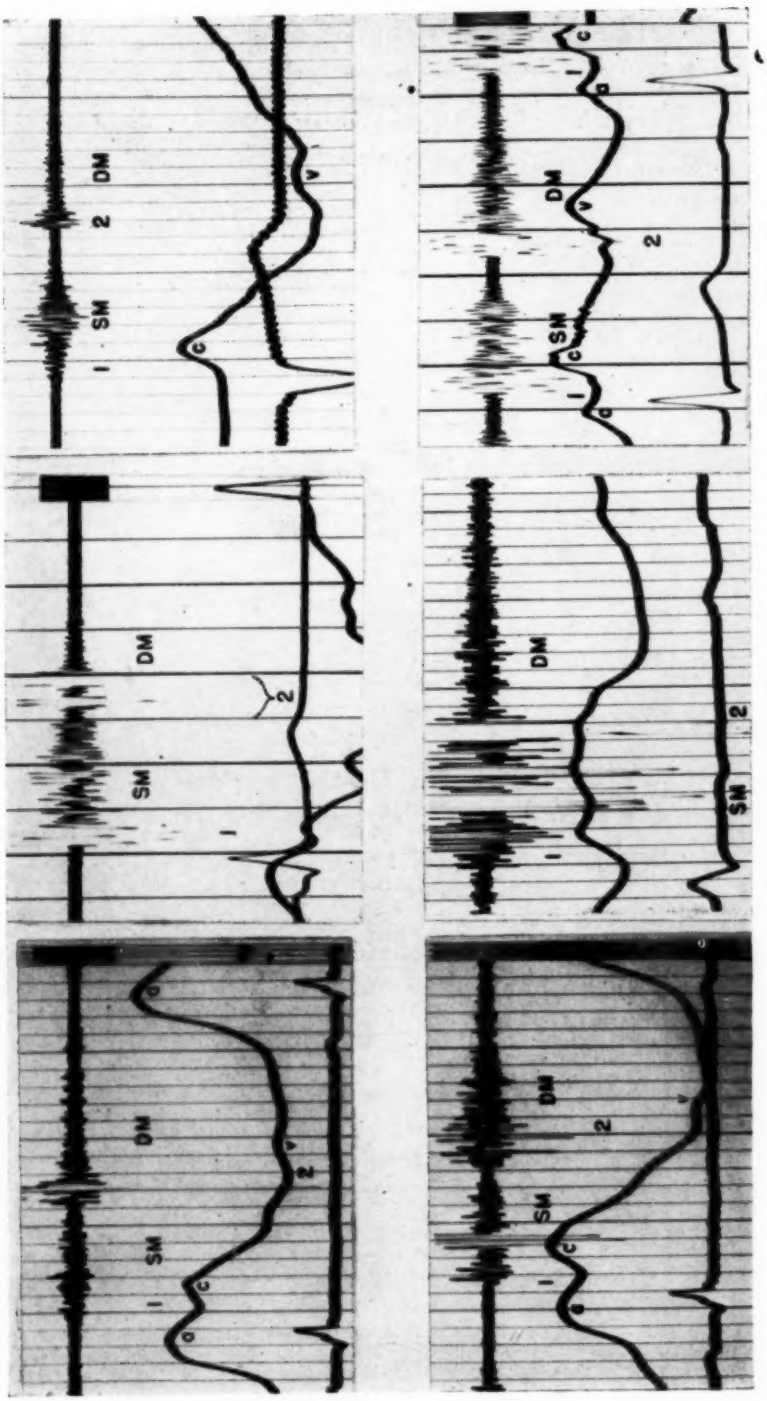
Fig. 1.—Artefacts (*A*) caused by lack of proper sealing of the lip of the open bell to the chest wall. *Upper tracing:* stethoscopic microphone with medium open bell over second left intercostal space. *Central tracing:* jugular pulse. *Lower tracing:* electrocardiogram, Lead I.
Note the standard sound *s* described in the text, which is used in subsequent illustrations.

Fig. 2.—Man, aged 46. Rheumatic heart disease following rheumatic fever at age 19. Mitral and aortic valvular disease.
Upper tracing: logarithmic microphone with large open bell over left sternal border in fifth intercostal space. *Central tracing:* jugular pulse. Because of free aortic regurgitation with marked arterial pulse in the neck, this tracing is almost wholly arterial. *Lower tracing:* electrocardiogram, Lead II.

Fig. 3.—Woman, aged 55. No history of rheumatic fever or syphilis. Admitted after sudden episode of shortness of breath during previous night. Diagnosis: syphilitic aortic insufficiency with Grade 4 aortic diastolic murmur.
Upper sound tracing: stethoscopic microphone with large open bell over the third left intercostal space. *Lower sound tracing:* logarithmic microphone with large open bell over the same area. *Reference tracing:* jugular pulse (mainly arterial because of the marked pulsation in the neck), and electrocardiogram, Lead I.



Figs. 4-8—*See opposite page for legends.*

the diastolic murmur contains few and insignificant low frequency components. It is well reproduced on the logarithmic tracing and is seen to have a quite definite crescendo-decrescendo configuration. It is difficult to explain why this quality of the murmur was not audible, for the intensity of the second sound is hardly sufficient to produce a fatiguing effect on the hearing mechanism. The fact that the diastolic murmur persists throughout diastole and is not merely an unsteady base line is proved by the short interval of silence prior to the second heart sound.

MODERATE BASAL DIASTOLIC MURMURS

The phonocardiograms of Grade 3 basal diastolic murmurs may show the purely decrescendo configuration which is the usual auscultatory character of these murmurs. Such tracings are shown in Figs. 4,*A* and 4,*B*, which also demonstrate the advantages of using the Bowles chestpiece. These tracings show how the Bowles chestpiece attenuates the first and second sounds and the systolic murmur, allowing a considerable increase in amplification, which enables better registration of the diastolic murmur. It is evident from both tracings that the murmur starts with the second heart sound and has a purely decrescendo configuration.

Duplication of the second sound at the base is usually attributed to asynchronous closure of the semilunar valves. If a diastolic murmur is present in such cases, phonocardiograms will show that the murmur follows either the first or second part of the split sound. However, as we shall demonstrate later, when the second sound is not duplicated there may be an interval of silence before the onset of the diastolic murmur. This fact, together with the frequent occurrence of a crescendo-decrescendo configuration of the murmur, would make

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Fig. 4.—Man, aged 43. No history of rheumatic fever or syphilis: Gradual shortness of breath for three months, ankle edema, and precordial pain on exertion. Grade 3 blowing diastolic murmur heard along left sternal border.

***A*, Logarithmic microphone with large open bell over second left intercostal space.**

***B*, Logarithmic microphone with Bowles chestpiece (0.015 inch diaphragm) at same location using greater amplification. Note that in *B* the band inscribed by the standard sound extends below the base line of the electrocardiogram.**

***Reference tracings:* jugular pulse and electrocardiogram, Lead I.**

Fig. 5.—Boy, aged 9. Rheumatic heart disease following rheumatic carditis at age 5. Grade 3 blowing diastolic murmur heard along left sternal border.

***Upper tracing:* logarithmic microphone with large open bell over second left intercostal space. *Central tracing:* jugular pulse. *Lower tracing:* electrocardiogram, Lead I.**

Fig. 6.—Man, aged 56. Repeated attacks of rheumatic fever at ages 8, 16, 26, and 40. Rheumatic heart disease found since last of these attacks. Congestive failure during last year. Grade 4 systolic and Grade 3 diastolic murmurs in second left intercostal space.

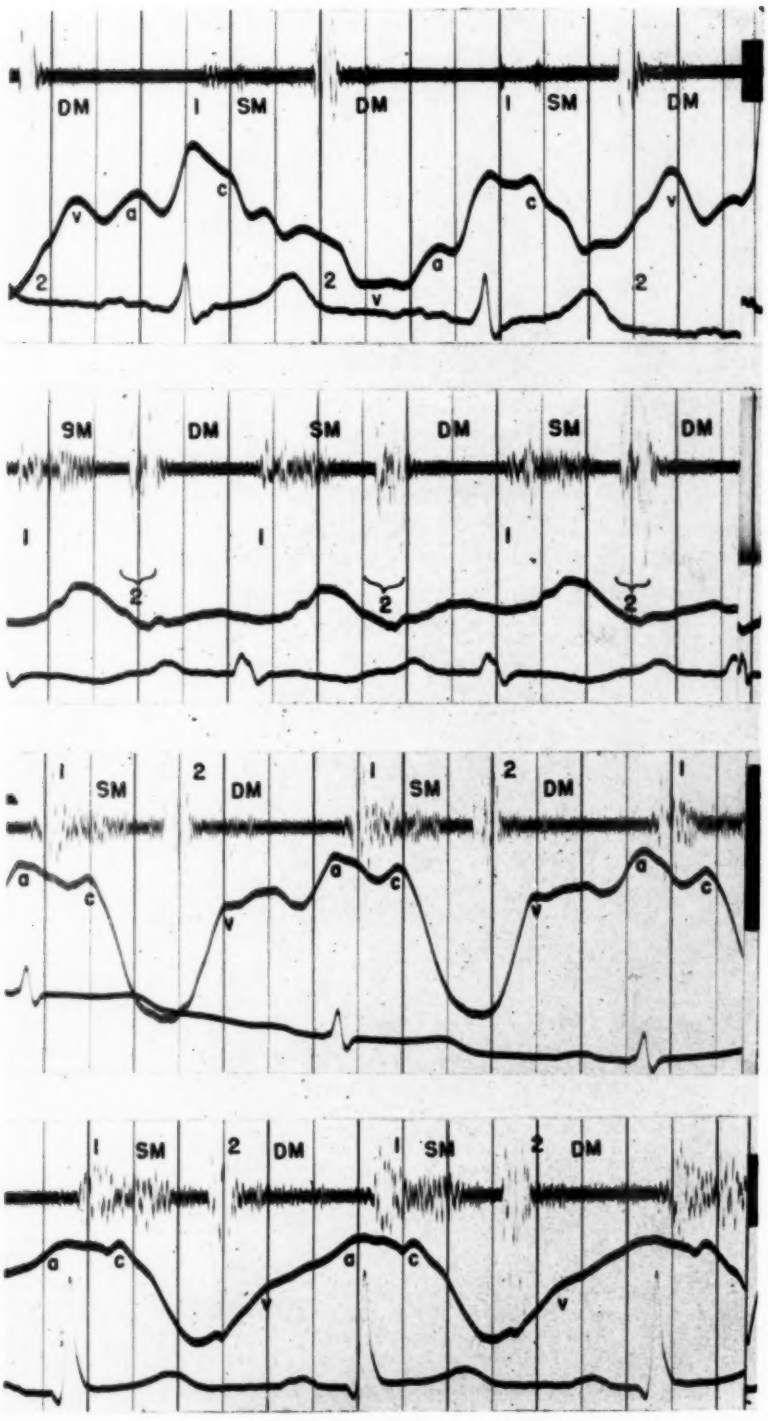
***Upper tracing:* logarithmic microphone with large open bell over second left intercostal space. *Central tracing:* jugular pulse. *Lower tracing:* electrocardiogram, Lead II.**

Fig. 7.—Man, aged 76. No history of rheumatic fever. Indefinite history of syphilis at age 30. Increasing exertional dyspnea for last two years with recent ankle edema. Heart greatly enlarged with Grade 3 diastolic murmur at second left intercostal space. Auricular fibrillation.

***Upper tracing:* logarithmic microphone with large open bell at second left intercostal space. *Central tracing:* jugular pulse. *Lower tracing:* electrocardiogram, Lead I.**

Fig. 8.—Boy, aged 6. Rheumatic heart disease with mitral and aortic involvement following rheumatic fever at age 4. Grade 2 systolic murmur masking first sound, and Grade 3 blowing diastolic murmur at second left intercostal space.

***Upper tracing:* logarithmic microphone with large open bell over second left intercostal space. *Central tracing:* jugular pulse. *Lower tracing:* electrocardiogram, Lead II.**



Figs. 9-12.—*See opposite page for legends.*

it unjustifiable to assume that the diastolic murmur was necessarily related to that part of the duplicated sound which immediately preceded it. The phonocardiogram of a moderate diastolic murmur following a duplicated second sound is shown in Fig. 5. This tracing presents a moderately coarse murmur starting with the latter part of a duplicated second sound and continuing in a decrescendo manner into diastole. Since there are a few vibrations between the components of the duplicated second sound, the murmur may be a crescendo-decrescendo murmur following the first component of the split sound. However, it is more probable that the murmur is related to the second part of the split sound.

The crescendo-decrescendo configuration found in loud diastolic murmurs is also found in phonocardiograms of moderate murmurs. Moderate basal diastolic murmurs in rheumatic and syphilitic aortic insufficiency showing this configuration are presented in Figs. 6, 7, and 8. The diastolic murmurs in these three tracings are somewhat similar, all being crescendo-decrescendo in configuration and of moderate frequency. The systolic murmurs in Figs. 7 and 8 end in early systole and thus provide a steady base line prior to the second heart sound, in contrast to which the diastolic murmurs stand out well.

SLIGHT BASAL DIASTOLIC MURMURS

On auscultation there may be some variation in character of the slight (Grade 2) basal diastolic murmur. This murmur is usually described as high-pitched and blowing but is occasionally coarse and low in pitch. Phonocardiograms of such murmurs show a greater degree of variation in frequency, configuration, and duration. Murmurs of moderately high frequency are shown in Figs. 9 and 10. In both of these tracings the vibrations constituting the murmur are low in amplitude. Their presence can be readily confirmed by contrasting the second half of diastole with the first. In addition, there is in Fig. 10 an interval of comparative silence between the systolic murmur and the second heart sound. The moderately high frequency vibrations which make up the

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Fig. 9.—Boy, aged 13. Rheumatic heart disease following acute rheumatism two years previously. Mitral and aortic insufficiency; congestive failure. Grade 2 blowing diastolic murmur along left sternal border.

Upper tracing: **logarithmic microphone with large open bell over second left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead II.**

Fig. 10. Girl, aged 16. Rheumatic heart disease since rheumatic fever at age 8. Possible additional patent auricular septum. Grade 2 blowing diastolic murmur along left sternal border. Grade 2 to 3 systolic murmur at pulmonary base with accentuated and duplicated second sound.

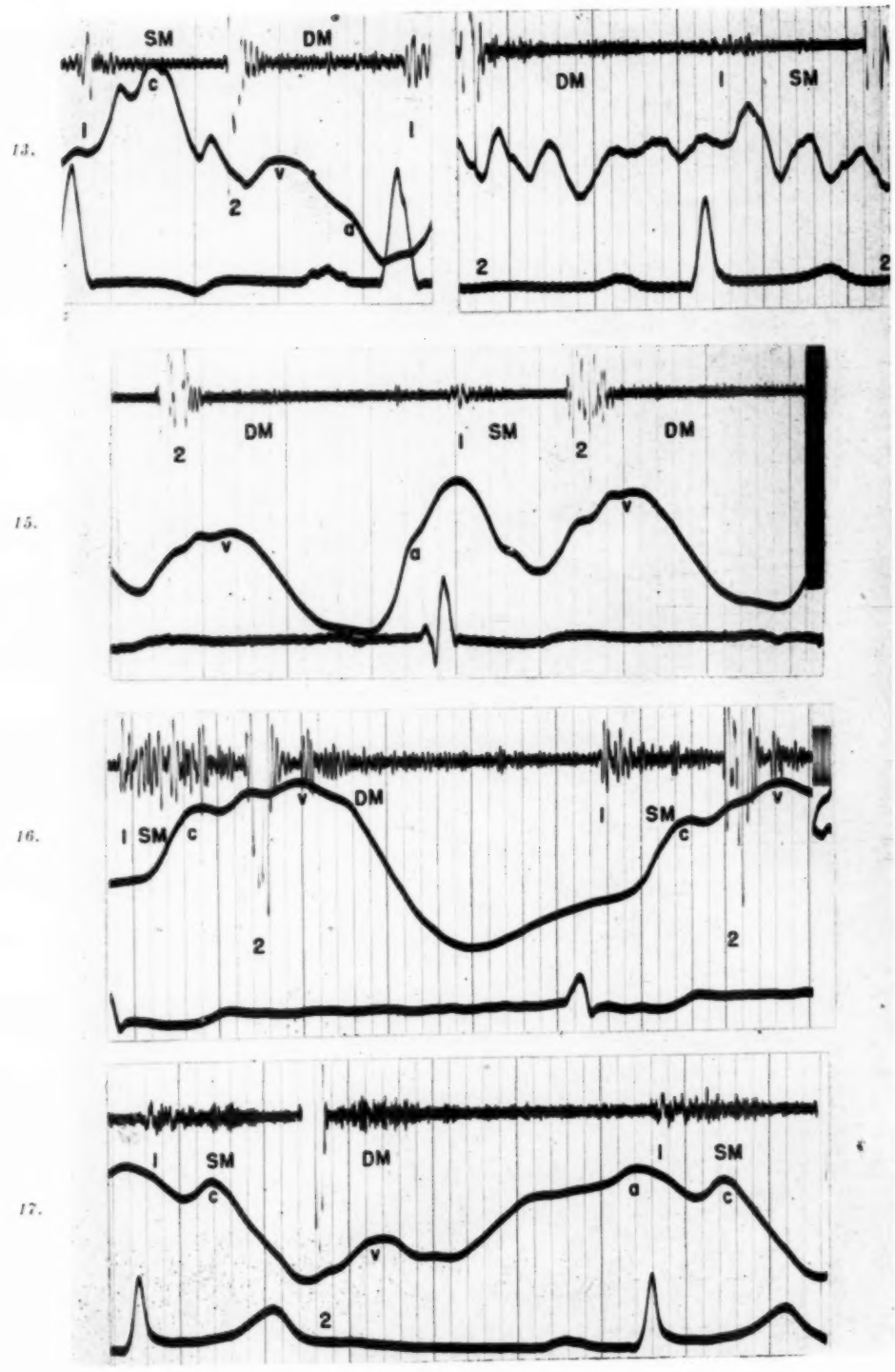
Upper tracing: **logarithmic microphone with Bowles chestpiece (0.015 inch diaphragm) over second left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead II.**

Fig. 11.—Boy, aged 14. Rheumatic heart disease following probable rheumatic fever at age 4, with recurrence at age 11. Grade 2 aortic diastolic murmur along left sternal border. Blood pressure 105/65.

Upper tracing: **logarithmic microphone with Bowles chestpiece (0.015 inch diaphragm) over fourth left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead II.**

Fig. 12.—Boy, aged 14. Rheumatic heart disease following rheumatic fever at age 8. Recurrences three years and again one month before tracing. Grade 2 blowing diastolic murmur along left sternal border.

Upper tracing: **logarithmic microphone with large open bell over second left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead II.**



Figs. 13-17.—*See opposite page for legends.*

diastolic murmur are seen to start not immediately with the second sound but after a short period of lower frequency vibrations. This may be explained by delay in the onset of regurgitation, due to momentary complete apposition of the valve cusps, following the turbulence set up by their closure.

Slight murmurs not noticeably different on auscultation from the murmurs in the two previous cases are shown in Figs. 11 and 12, although it is apparent from these phonocardiograms that the murmurs are composed of vibrations of somewhat lower frequency. The presence of a diastolic murmur in these tracings is decided by the greater amplitude of the vibrations in early diastole, in contrast to less intense vibrations both in late diastole and in late systole. The diastolic murmur in both cases has a crescendo-decrescendo configuration which varies somewhat with each cardiac cycle. In Fig. 13 the diastolic murmur is of moderately low frequency. It starts a short interval after the second heart sound and is then continuous throughout diastole. It can be contrasted with the systolic vibrations which are lower in intensity, especially just before the second sound. No systolic murmur was heard on auscultation. The diastolic murmur was blowing in quality and not unusual in character.

Although it is usual for the basal diastolic murmur to become minimal toward the end of diastole, this is not necessarily so, even in the slight (Grade 2) murmur. Figs. 14 and 15 show murmurs which continue throughout diastole without much diminution in intensity. In both of these tracings the diastolic murmur continues up to the time of the first heart sound and may be contrasted with vibrations of lesser intensity in the latter part of systole. In neither of these tracings is the decrescendo nature of the murmur at all marked.

The phonocardiogram of a patient with pulmonary regurgitation which shows a very different configuration is seen in Fig. 16. This tracing is of in-

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Fig. 13.—Man, aged 23. Rheumatic heart disease following acute rheumatism complicating scarlet fever at age 12. Heart considerably enlarged with Grade 2 diastolic murmur along left sternal border.

Upper tracing: **logarithmic microphone with large open bell over third left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead II.**

Fig. 14.—Woman, aged 22. Rheumatic heart disease following attacks of rheumatic fever at ages 9, 11, and 12. Minimal cardiac enlargement with Grade 2 aortic diastolic murmur along left sternal border. No diastolic murmur at apex.

Upper tracing: **logarithmic microphone with Bowles chestpiece (0.015 inch diaphragm) over fourth left intercostal space after exercise.** ***Central tracing:*** **linear phonocardiogram at apex.** ***Lower tracing:*** **electrocardiogram, Lead II.**

Fig. 15.—Man, aged 74. Syphilis at age 35. Recent congestive failure with some hypertension. Grade 2 blowing early diastolic murmur in third left intercostal space following accentuated second sound. Rumbling diastolic murmur just medial to apex. Fluoroscopy revealed hilar dance without increase in aortic pulsation. Blood pressure 160/85. Diastolic murmur probably due to pulmonary regurgitation.

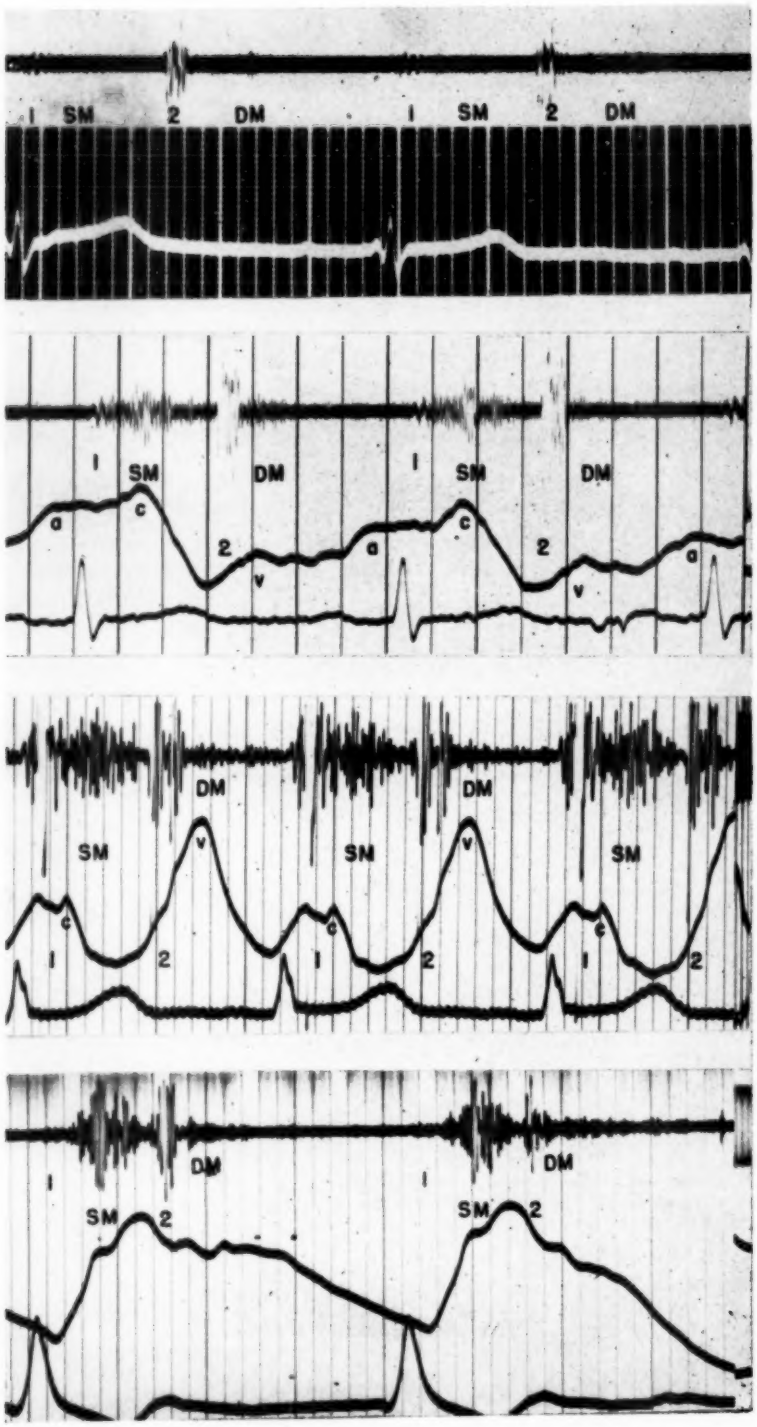
Upper tracing: **logarithmic microphone with large open bell over fourth left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead I.**

Fig. 16.—Man, aged 28. Rheumatic heart disease without known rheumatic fever or chorea. Mitral and probably tricuspid stenosis; auricular fibrillation; congestive failure. Variable low-pitched Grade 2 blowing diastolic murmur localized to second left intercostal space, attributed to pulmonary regurgitation.

Upper tracing: **logarithmic microphone with large open bell over second left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead I.**

Fig. 17.—Boy, aged 15. Rheumatic heart disease following rheumatic fever at age 11. Heart border line in size. Grade 2 blowing diastolic murmur along left sternal border and quite widely conducted. No mitral diastolic murmur.

Upper tracing: **logarithmic microphone with Bowles chestpiece (0.015 inch diaphragm) at second left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead II.**



Figs. 18-21.—*See opposite page for legends.*

terest in that the diastolic murmur, which is of decrescendo type, appears to follow the latter part of a widely split second sound. By reference to the apex cardiogram it was found that the A-V opening occurred before the second part of the split sound was inscribed. This part of the sound is therefore probably not an opening snap and can be attributed to a delayed closure of the aortic valve following an earlier and accentuated sound of pulmonary valve closure. If this hypothesis is correct and if the diastolic murmur is due to pulmonary regurgitation, then it must be fortuitous that the murmur appears to originate with the latter part of the duplicated second sound. In other words, the latter sound must be inscribed on the beginning of a diastolic murmur of delayed onset, with, perhaps, a crescendo-decrescendo configuration.

Phonocardiograms of slight basal diastolic murmurs will occasionally show the conspicuous crescendo-decrescendo configuration seen with louder murmurs. Such a tracing is shown in Fig. 17, which is taken from a patient in whom the diastolic murmur was not noted on auscultation to be of unusual character. However, there is a progressive increase in the intensity of the murmur up to about the time of the apex of the V wave in the phlebogram, when it is followed by a fairly marked reduction in intensisty.

VERY SLIGHT BASAL DIASTOLIC MURMURS

The very slight murmur of aortic or pulmonary regurgitation is the murmur which has hitherto proved the most difficult to register. Especially has this been so when the murmur was not only extremely faint but also very high in pitch. Such circumstances existed at the time of the tracing shown in Fig. 18. In this patient the murmur was barely audible with the use of an acoustic stethoscope and a Bowles chestpiece of usual thickness (0.015 inch). It was considerably more pronounced when heard through the audiophones with the phonocardiograph amplifier and the Bowles chestpiece with a thick diaphragm (0.035 inch). This illustrates the circumstances in which the Bowles chestpiece

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Fig. 18.—Man of middle age with syphilitic aortitis and dextrocardia. Grade 1 high-pitched diastolic murmur only just above threshold of audibility.

Upper tracing: **logarithmic microphone with Bowles chestpiece with thick diaphragm (0.035 inch) over area of maximal intensity.** ***Lower tracing:*** **electrocardiogram, Lead II.**

Fig. 19. Girl, aged 14. Rheumatic heart disease following rheumatic fever three years and again five months previously. Grade 2 systolic and Grade 1 blowing diastolic murmurs heard in third left intercostal space.

Upper tracing: **logarithmic microphone with Bowles chestpiece (0.015 inch diaphragm) over third left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead II.**

Fig. 20.—Girl, aged 10. Pains in legs at age 4, when moderate systolic murmur over left sternal border was found. Slight cardiac enlargement at time of tracing with Grade 3 systolic and Grade 1 diastolic murmurs at second left intercostal space. Probably congenital rather than rheumatic heart disease.

Upper tracing: **logarithmic microphone with large open bell over fourth left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead II.**

Fig. 21.—Man, aged 50. No history of rheumatic fever. Known hypertension for five months; recent congestive failure. Grade 4 systolic murmur with thrill over aortic area, and Grade 1 diastolic murmur. Because of definite rumbling apical diastolic murmur, rheumatic as well as hypertensive heart disease was diagnosed.

Upper tracing: **logarithmic microphone with large open bell at second left intercostal space.** ***Central tracing:*** **jugular pulse. Tracing mostly carotid because of marked arterial pulsation in neck.** ***Lower tracing:*** **electrocardiogram, Lead I.**

with a thick diaphragm when used in conjunction with an electronic amplifier is of definite value. It should be emphasized that this is of no value in the acoustic stethoscope, as amplification is essential when a diaphragm of such thickness is used. The murmur is seen to start a short interval after the second sound and is of rather high frequency and crescendo-decrescendo in configuration. The second sound in this patient was of considerable intensity and would therefore produce a fatiguing effect on the hearing mechanism, which, persisting for a short period in diastole, would tend to mask the murmur.

The tracing of a second patient with a very slight basal diastolic murmur is shown in Fig. 19. In this case the murmur was satisfactorily registered by use of the Bowles chestpiece with a thin diaphragm. The murmur is crescendo-decrescendo in configuration, being maximal shortly after an accentuated second sound, at about the time of the apex of the V wave in the jugular phlebogram. It is of moderate frequency, being lower in frequency than the murmur in Fig. 18.

The relationship of a very slight murmur to a duplicated second sound is illustrated by Figs. 20 and 21. The first of these tracings (Fig. 20) shows a duplicated second sound and a crescendo-decrescendo diastolic murmur, with maximal intensity at the apex of the V wave of the phlebogram. The systolic murmur usually terminates just prior to the second sound. The second tracing (Fig. 21) demonstrates that the onset of the diastolic murmur may in some cycles be separated from the second sound by a short, silent interval. If there had been duplication of the second sound in this case, and if the murmur had been related to the first part of the split sound, then it might have appeared sometimes to start only with the second component. It should be noted that the diastolic murmur is well recorded in this tracing, although it was very slight on auscultation. This is probably explained by the considerable intensity of the systolic murmur and second sound, which would cause fatigue of the hearing mechanism for a short period in early diastole when the diastolic murmur is most intense.

DIASTOLIC MURMURS WHICH ARE QUESTIONABLE ON AUSCULTATION

In the four patients with very slight basal diastolic murmurs whose tracings are illustrated, there was in each case a difference of opinion as to whether the murmur was present or not. Some observers had in every instance failed to hear the murmurs. Even greater uncertainty was expressed in the case of the patient whose tracing is shown in Fig. 22. In this tracing the fourth component of the second sound, the A-V opening sound, can be clearly seen. Between this sound and the third sound there is a regular series of moderately fine vibrations which constitute a diastolic murmur. The reason this diastolic murmur was not heard with certainty on auscultation is that the great intensity of the systolic murmur and the second component of the second sound would cause a fatiguing effect on the hearing mechanism during early diastole.

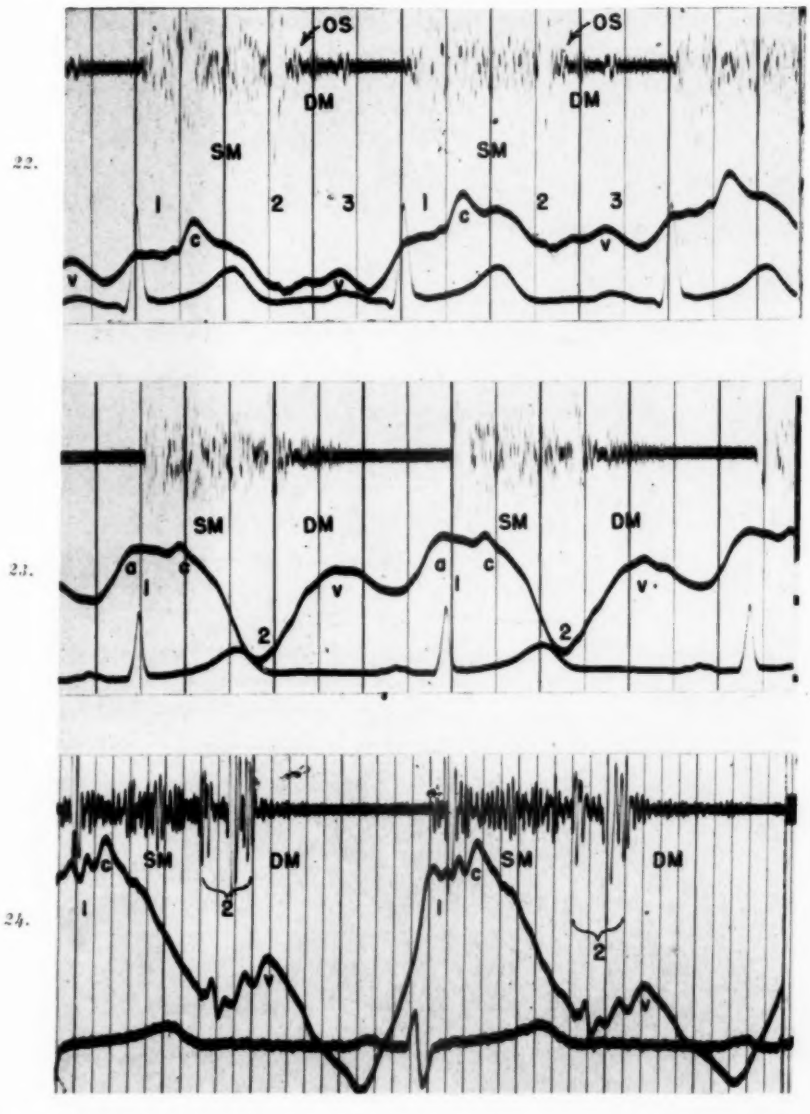


Fig. 22.—Girl, aged 15. Rheumatic heart disease following recurrent attacks of rheumatic fever during last two years. Grade 3 systolic murmur at fourth left intercostal space with questionable, very slight diastolic murmur.

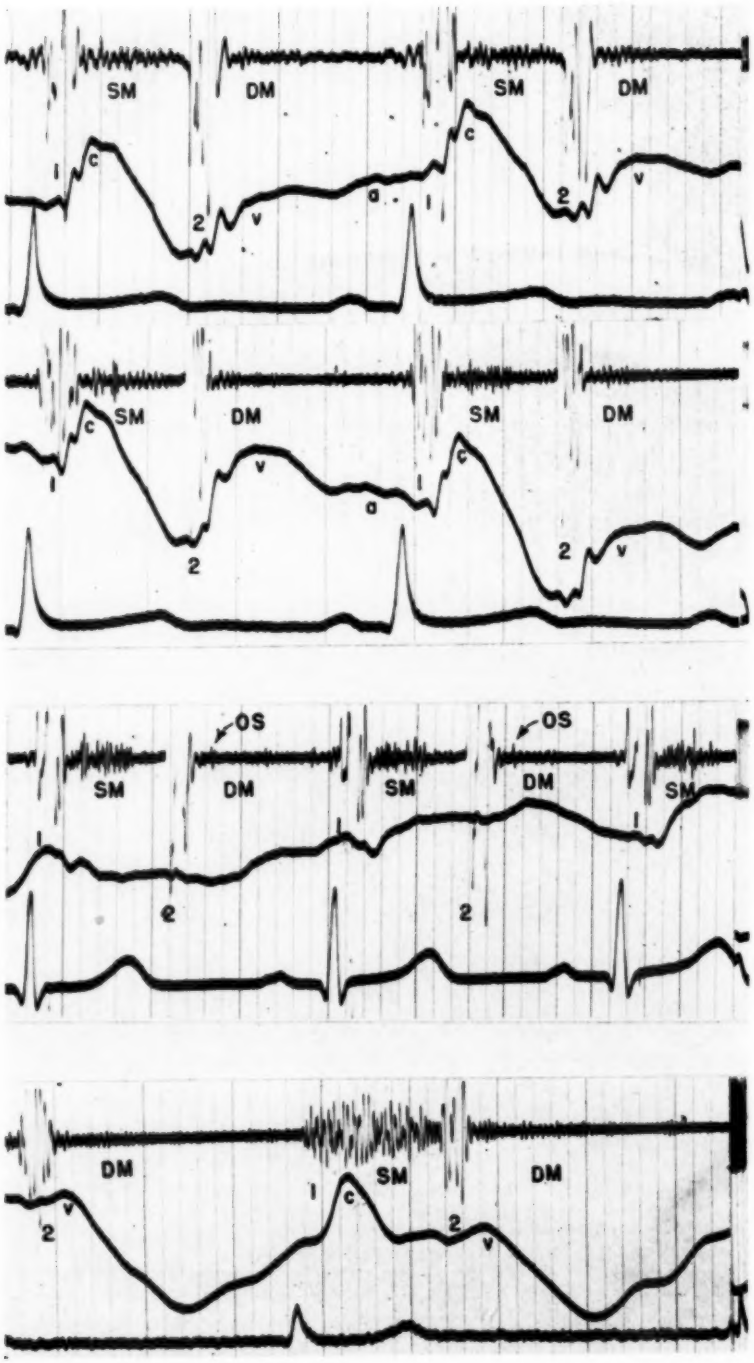
Upper tracing: logarithmic microphone with large open bell at fourth left intercostal space. *Central tracing:* jugular pulse. *Lower tracing:* electrocardiogram, Lead II.

Fig. 23.—Girl, aged 7. Acute rheumatic fever following febrile cold two months previously. Grade 3 systolic murmur at third left intercostal space with scratchy murmur in diastole which was thought by some observers to be friction rub, and by others rather harsh murmur of aortic regurgitation.

Upper tracing: logarithmic microphone with Bowles chestpiece (0.015 inch diaphragm) over third left intercostal space. *Central tracing:* jugular pulse. *Lower tracing:* electrocardiogram, Lead II.

Fig. 24.—Boy, aged 15. No history of rheumatic fever. Moderate rachitic deformity of chest; heart normal in size. Grade 3 systolic murmur and accentuated second sound at second left intercostal space. No diastolic murmur heard. Murmur considered probably physiological.

Upper tracing: logarithmic microphone with large open bell over second left intercostal space. *Central tracing:* jugular pulse. *Lower tracing:* electrocardiogram, Lead I.



Figs. 25-27.—*See opposite page for legends.*

DIFFERENTIAL DIAGNOSIS FROM PERICARDIAL FRICTION RUB

It is usually quite simple to differentiate a friction rub from the diastolic murmur of aortic regurgitation. In doubtful cases the phonocardiogram may be of some help, since it provides evidence that can be analyzed more carefully than the sounds heard on auscultation. The phonocardiogram in Fig. 23 is of a patient in whom a rather scratchy diastolic sound was heard, and there was some question as to whether aortic regurgitation was present. The diastolic murmur is very clearly demonstrated by the tracing. Its onset is separated from the second sound by a short period of silence and corresponds to the time of opening of the A-V valves. The murmur is of moderate frequency and diminuendo configuration. These characteristics are frequently found in the murmur of aortic regurgitation; they would favor an interpretation on this basis rather than that of pericardial friction rub.

BASAL DIASTOLIC VIBRATIONS WHERE NO MURMUR WAS AUDIBLE ON AUSCULTATION

The following six phonocardiograms were found among tracings on 200 patients in whom further study of auscultatory findings was thought to be desirable. They were the only tracings in which diastolic vibrations considered to be of significance were located at the base of the heart in the absence of any audible murmur. Vibrations of significance are those which recur regularly in each cardiac cycle, to which they have a definite relation manifested by a period of maximal or minimal intensity. Other variations in the base line may be due to noises in the room where the phonocardiograms are recorded, or they may be produced by involuntary muscular movements of the chest wall; these base-line variations will be unrelated to the cardiac cycle. The tracings in Figs. 24 25 were made from patients in whom no diastolic murmur was heard at apex or base.

The tracing in Fig. 24 shows that the second sound is in actual fact widely split. The first element of the sound was not identified clinically, probably because it is continuous with the systolic murmur. In diastole there are vibrations of decrescendo configuration and moderately low frequency continuing almost to the first sound. The reason no diastolic murmur was heard is partly that the vibrations are of comparatively low frequency, occurring in a region of the auscultatory spectrum in which acuity of hearing is reduced. In addition,

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Fig. 25.—Girl, aged 14. Rheumatic fever at age 4. Gradual development of Grade 2 apical systolic murmur during last seven years. No diastolic murmur heard. X-ray films show enlargement of left auricle.

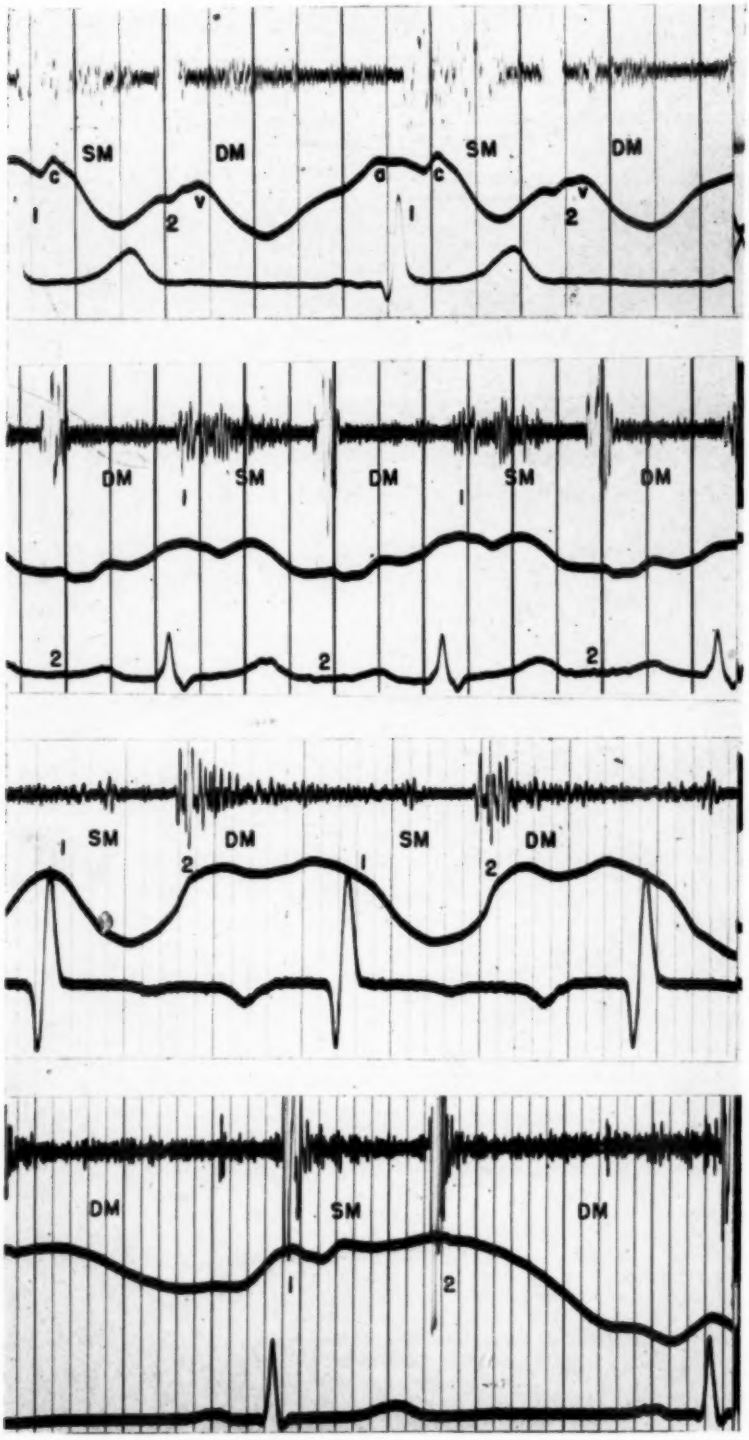
Upper sound tracing: **stethoscopic microphone with large open bell over second left intercostal space.** ***Lower sound tracing:*** **logarithmic microphone with large open bell over same area.** ***Reference tracing:*** **jugular pulse, and electrocardiogram, Lead II.**

Fig. 26.—Boy, aged 4. Recent purpura accompanied by joint pains. Grade 2 to 3 apical systolic murmur and questionable apical diastolic murmur. No basal diastolic murmur was heard.

Upper tracing: **logarithmic microphone with large open bell at second left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead II.**

Fig. 27.—Woman, aged 62. Arteriosclerotic heart disease; auricular fibrillation; moderate anemia; congestive heart failure. Rather rough systolic murmur at base, but no diastolic. Questionable apical diastolic murmur.

Upper tracing: **logarithmic microphone with large open bell over second right intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead I.**



Figs. 28-31.—*See opposite page for legends.*

the loud systolic murmur and accentuated second sound would together exert a considerable fatiguing effect on the hearing mechanism which would persist through early diastole. Because of the moderate intensity and decrescendo configuration of the vibrations, they should probably be considered of a significance similar to that of an audible diastolic murmur. In this patient they would, therefore, suggest pulmonary insufficiency.

The tracings of Fig. 25 show vibrations starting in early diastole and becoming minimal prior to the auricular vibrations. They are of rather low frequency and are seen both in the stethoscopic and logarithmic recordings. The reason that no murmur was audible is probably the combination of low frequency with the masking effect of a loud second sound. Vibrations of this character have not been found in phonocardiograms of normal persons, but further experience must be obtained before they can be related to anatomical or physiological abnormalities of the heart.

Phonocardiograms of three patients were taken because question of an apical diastolic murmur had been raised. In all of these an apical diastolic murmur was recorded, but there were definite diastolic vibrations of different character at the base of the heart. The records are shown in Figs. 26, 27, and 28. The tracing in Fig. 26 shows definite vibrations at the time of the opening of the A-V valves. During early diastole there are vibrations of low intensity which can be contrasted with the comparatively steady base line at the very end of systole. The vibrations have no other characteristic configuration and their significance is unknown. In the phonocardiogram in Fig. 27 there are distinct vibrations of rather low frequency and intensity which are maximal in early diastole. At this period of the cardiac cycle there would probably be on auscultation some fatiguing of the hearing mechanism following the long, harsh systolic murmur and moderate second sound. This would explain why no murmur was audible. However, we must have further experience before we may interpret such vibrations as definitely indicative of valvular insufficiency. In Fig. 28 there is a short period of quiet at the end of systole in contrast to

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Fig. 28.—Girl, aged 8. Probable rheumatic heart disease since rheumatic fever one year previously. Grade 2 apical systolic with questionable apical diastolic murmur. No basal diastolic murmur.

Upper tracing: **logarithmic microphone with large open bell at second left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead II.**

Fig. 29.—Girl, aged 10. Rheumatic heart disease following chorea at age 8 and rheumatic fever at age 9. Diastolic and presystolic murmurs heard at apex but no diastolic murmur at base.

Upper tracing: **logarithmic microphone with large open bell over second left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead II.**

Fig. 30.—Woman, aged 27. Short of breath since childhood. Progressive cyanosis, clubbing of fingers, and markedly increasing dyspnea during previous twelve months. Grade 3 diastolic murmur of unusual rumbling quality localized to third left intercostal space following markedly accentuated second sound.

Upper tracing: **logarithmic microphone with large open bell at third left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead I (upside down because of misplaced lead wires).**

Fig. 31.—Woman, aged 24. No known rheumatic fever or heart disease. Diastolic murmur over lower central sternum, of rather coarse, blowing character, heard first during pregnancy. Following delivery murmur was less intense and rather more continuous in nature. Blood pressure, 110/70. No abnormality of heart on fluroscopy. Murmur was considered to be a mediastinal hum.

Upper tracing: **logarithmic microphone with large open bell in third left intercostal space.** ***Central tracing:*** **jugular pulse.** ***Lower tracing:*** **electrocardiogram, Lead II.**

which the diastolic vibrations are particularly apparent. They are crescendo-decrescendo in configuration, being maximal shortly after the apex of the V wave of the jugular phlebogram, and they continue throughout diastole. It is more difficult in this case than in the preceding to explain why no murmur was audible, though once again it is probable that the intensity of the systolic murmur and second sound exerted some fatiguing effect on the hearing mechanism. The moderate intensity and characteristic configuration of the vibrations in this patient would suggest aortic or pulmonary insufficiency.

Fig. 29 shows throughout diastole vibrations of moderate frequency and greater intensity than those in the quiet interval just preceding the second sound. The vibrations differ in configuration from those recorded at the apex where there was a period of quiet before the A-V opening and definite presystolic accentuation. The absence of a basal murmur on auscultation may have been due to the fatiguing effect of a rather loud second sound.

DIASTOLIC MURMURS OF UNUSUAL CHARACTER

An unusually coarse decrescendo diastolic murmur of moderately high intensity is present in Fig. 30. The murmur persists throughout diastole and can be contrasted with the comparative silence of the latter half of systole. The patient died a few months after the phonocardiogram was taken. It was expected that on post-mortem examination some form of congenital heart disease might be found, but there was no congenital defect. Marked right-sided hypertrophy secondary to pulmonary endarteritis was present, and the pulmonary artery was dilated and atheromatous. The diastolic murmur in this patient must be explained on the basis of pulmonary insufficiency due to pulmonary hypertension and dilatation of the pulmonary artery.

In Fig. 31 there is a decrescendo diastolic murmur coming off the second sound, followed by a gradual crescendo murmur through the remainder of diastole. The latter part is consistent with a mediastinal hum, but the early decrescendo phase would suggest the additional diagnosis of aortic or pulmonary regurgitation. However, the clinical features of this case make such a decision difficult.

THE DIASTOLIC MURMUR OF RETROVERTED AORTIC CUSP

The loud musical murmur of retroversion of one or more cusps of the aortic valve has long been recognized. Bellet and others,[15] who published a phonocardiogram of one of these cases, have discussed the mechanism of its causation. One patient under our observation was found to have a very loud diastolic murmur of characteristic quality which later disappeared, leaving only a moderate murmur of aortic insufficiency. Tracings before and after the disappearance of the murmur are shown in Fig. 32. The marked and rapid change in this murmur gives strong support to the theory that the murmur is due to retroversion of an aortic valve cusp. In this case the retroverted cusp apparently underwent spontaneous return to its normal position, leaving some evidence of underlying aortic valve disease with aortic insufficiency.

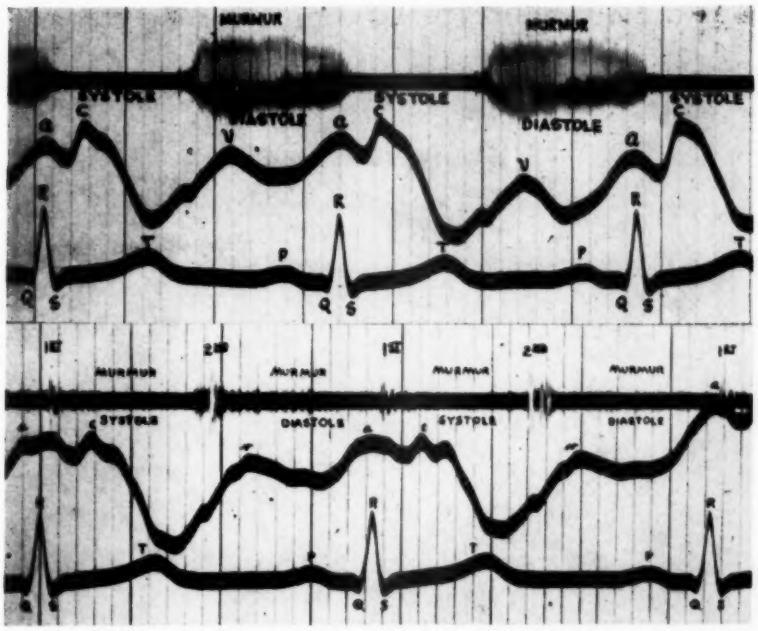

Fig. 32.—Boy, aged 16. After nine days of acute rheumatic fever suddenly developed Grade 6 diastolic murmur in aortic area, of "seagull" type with thrill. This lasted fourteen weeks and suddenly decreased to Grade 3 without thrill.

Upper sound tracing: logarithmic microphone with large open bell over aortic area. *Lower sound tracing:* logarithmic microphone with Bowles chestpiece (0.015 inch diaphragm) over same area some weeks later, when murmur had undergone sudden decrease in intensity. *Reference tracings:* jugular pulse and electrocardiogram, Lead I.

The musical quality and great intensity of the diastolic murmur shown in Fig. 33 suggested the diagnosis of retroversion of an aortic cusp. The diastolic murmur in these tracings has a fundamental frequency of about 200 cycles per second. It is more intense and higher in pitch than the systolic murmur. Its configuration approximates an exponential decrement, which is a reduction in amplitude such as occurs when a tight string is plucked.

The phonocardiogram in Fig. 34 is taken from another patient in whom the diagnosis of retroversion of an aortic valve cusp was made. The diastolic murmur is of greater intensity than the second sound, from which it can be separated by a slight splitting effect. This murmur, like that in the previous case, has the decrement similar to that obtained by plucking a string.

The exact mechanism of the production of the musical diastolic murmur in these cases is not fully understood. It is almost certainly the valve cusp itself which undergoes vibrations initiated by the closure of the semilunar valves and maintained by the hemodynamics of the regurgitant stream for a greater or lesser time. It is interesting that a musical second sound may occur in the absence of aortic regurgitation or of retroversion of an aortic cusp. Such a case is illustrated in Fig. 35. This phonocardiogram was not considered to show a

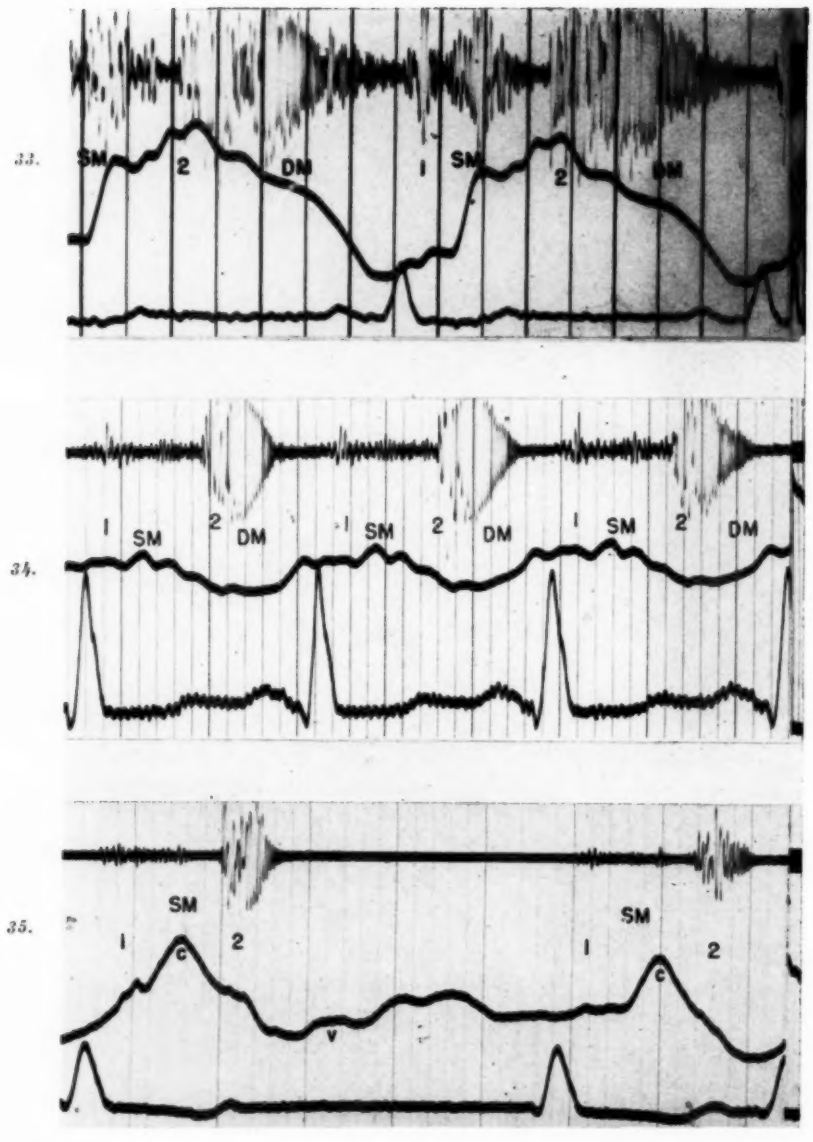

Fig. 33.—Woman, aged 21. Rheumatic heart disease following recurrent attacks of rheumatic fever since age 8. Aortic regurgitation diagnosed at age 11. Signs of retroversion of aortic cusp at age 19. Successful treatment of subacute bacterial endocarditis at age 20, with increase in diastolic murmur. At time of phonocardiogram thrill accompanied Grade 5 diastolic murmur of whining, high-pitched character.

Upper tracing: logarithmic microphone with large open bell over second left intercostal space. *Central tracing:* jugular pulse. *Lower tracing:* electrocardiogram, Lead II.

Fig. 34.—Man, aged 27. Rheumatoid arthritis since age 19. Musical diastolic murmur first heard at age 22, with little variation during last five years. Second sound metallic in quality followed by high-pitched musical diastolic murmur.

Upper tracing: logarithmic microphone with large open bell over second left intercostal space. *Central tracing:* jugular pulse. *Lower tracing:* electrocardiogram, Lead I.

Fig. 35.—Woman, aged 54. Chronic pyelonephritis, uremia, congestive heart failure, auricular fibrillation, cardiac enlargement. Blood pressure, 140/90. Musical "cardboard door" second sound at aortic base, with no diastolic murmur.

Upper tracing: logarithmic microphone with large open bell over second right intercostal space. *Central tracing:* jugular pulse. *Lower tracing:* electrocardiogram, Lead I.

diastolic murmur, for the musical second sound terminated by the time of opening of the A-V valves, as judged by the apex cardiogram. However, the configuration of the sound is so similar to that found in the musical diastolic murmurs shown above that great care must be taken not to confuse the two. It is possible that this similarity may throw some light on the mechanism of their formation.

SUMMARY AND CONCLUSIONS

1. The ideal phonocardiograph should have the following characteristics:

a. Adequate sensitivity and deflection speed to record the faint, high-pitched murmurs encountered in auscultation.

b. A frequency response which enables sufficient amplification to register these murmurs without excessive deflections from vibrations of lower frequency. Such a response is present when the intensity of the vibrations undergoes the same modification with regard to frequency as occurs in the average stethoscope, in conjunction with the average hearing mechanism. This response has been termed "logarithmic."

c. An alternative frequency response, which will allow better reproduction of the lower frequency vibrations. This is available in the response which has been termed "stethoscopic."

d. Modifying characteristics that are obtained from the open bell and the Bowles diaphragmatic chestpieces, which may be added to either logarithmic or stethoscopic response.

2. Failure to comply with these requisites has resulted in inability to record the faint, high-pitched basal diastolic murmurs, and as a result there has been no adequate description of the graphic configuration of basal diastolic murmurs.

3. The physiological and physical factors concerned in the production of basal diastolic murmurs are discussed, in order that they may be related to the characteristics of the murmurs as recorded by the phonocardiograph.

4. The auscultatory characteristics of the basal diastolic murmurs are enumerated and a quality not previously brought to notice is described. This is a crescendo-decrescendo quality in early diastole which is sometimes obvious on auscultation but much more frequently demonstrated by phonocardiography.

5. A phonocardiographic technique which has proved satisfactory for the registration of all heart sounds and murmurs is described. By use of this technique all basal diastolic murmurs heard on auscultation can be recorded, with occasional registration of basal diastolic vibrations where no murmur was audible.

6. A method of standardization of the intensity of heart sounds and murmurs is described. This method is used in the illustrations.

7. Continuous murmurs caused by patent ductus, arteriovenous aneurysm, and venous hum are excluded from this study. The graphic configuration of other basal diastolic murmurs is illustrated by tracings from twenty patients with murmurs varying from very slight to loud in intensity. The characteristics of these murmurs are as follows:

a. The onset of the murmur can frequently be distinguished quite readily from the end of the second component of the second sound, although sometimes the two may be fused. The onset of the murmur may be separated from the second sound by a short silent interval or a series of lower frequency vibrations, due perhaps to the third component of the second sound. Such a delay is more frequently seen in murmurs of low intensity.

b. When the second sound is duplicated, the murmur is seen to come off one or other component of the sound. Such duplicated second sounds may represent asynchronism of closure of the semilunar valves. However, it is pointed out that, because of the variable onset and configuration of the diastolic murmur, it is unwise to assume that a murmur appearing to commence with the latter part of a duplicated sound is necessarily related to the semilunar closure that is delayed.

c. The frequency of the vibrations constituting the murmur varies in different cases from moderately low to high.

d. A purely decrescendo configuration is seen in only five of the twenty tracings. The other fifteen show to varying extents a crescendo-decrescendo configuration, with maximal intensity at or shortly after the time of the apex of the V wave in the jugular phlebogram.

e. The murmur sometimes ends in early diastole but in the majority of cases may be traced up to the first sound of the next cardiac cycle.

f. There is frequently a short period in late systole of comparative silence, in contrast to which the diastolic murmur is clearly evident.

8. The presence of a diastolic murmur is demonstrated in a patient who had on auscultation a very questionable murmur.

9. The differential diagnosis of a scratchy aortic diastolic murmur from a pericardial friction rub is made in another patient.

10. Vibrations of the base line may occur in diastole from extracardiac sources of activity. These vibrations should not be considered to be significant unless they show some period of maximal or minimal intensity which is related to the cardiac cycle, or some other obvious characteristic that is found in consecutive cardiac cycles.

11. Phonocardiograms of six patients are shown in which significant diastolic vibrations were recorded, although no murmur was heard on auscultation. The origin of these vibrations and the reasons they were not heard are discussed. The reasons are usually two, namely: (a) the low intensity of the vibrations with regard to their frequency; and (b) the fatiguing effect of a loud systolic murmur and second sound on the hearing mechanism.

12. The phonocardiogram of a loud and unusually low-pitched diastolic murmur found in a patient with pulmonary regurgitation is shown. Another unusual murmur believed, by auscultation, to be a mediastinal hum had, on phonocardiography, an early decrescendo phase suggestive of aortic or pulmonary regurgitation.

13. The phonocardiograms of three patients with retroversion of aortic cusps are shown. In one of these the characteristic loud murmur disappeared

under observation; this was considered to be evidence of spontaneous correction of the retroversion and confirmatory of the diagnosis.

14. The mechanism of production of the musical diastolic murmur in retroversion of an aortic cusp is discussed, and the similarity of the phonocardiogram to that of a musical second sound is noted.

15. When auscultation of a patient produces doubt or difference of opinion as to whether a basal diastolic murmur is present or not, this important question may be decided by an adequate phonocardiogram.

16. The configurations of the murmurs recorded show considerable variation but conform to certain distinct patterns.

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SOME EFFECTS ON THE CIRCULATION OF SMOKING CIGARETTES WITH VARYING NICOTINE CONTENT

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IT IS generally agreed that the smoking of cigarettes produces immediate changes in the circulation in practically all persons. The effects are shown by an increase in heart rate and blood pressure as well as by constriction of the peripheral vessels.[1] In some patients the occurrence of vasospasm has been reported in coronary and retinal arteries.[2,3] Variability in the degree of response in different subjects depends to a greater degree on individual susceptibility to tobacco than on the presence of cardiovascular disease.[4] Most investigators have ascribed to the nicotine in the smoke the chief role in producing these vascular reactions.[5,6,7] Some, however, still question its importance in this respect, and the suggestion has been made that sympathetic stimulation brought about by the irritating action of the smoke upon the respiratory tract may be responsible for the changes noted.[8] Others have attributed the effects to deep breathing.[9]

Such varying opinions leave the issue still unsettled. Because the matter is of some practical importance, particularly for patients with cardiovascular diseases, this study was planned.

MATERIAL AND METHODS

Observations were made on seventeen subjects. In nine, no cardiovascular disease was present. Of these, three were men and six were women. Their ages ranged from 22 to 56, with an average of 34 years. There were eight patients with cardiovascular disease, of whom six were men and two were women. Their ages ranged from 34 to 57, with an average of 47 years. In six, the diagnosis was coronary heart disease with anginal pain; one of these also had hypertension and three showed evidence of healed cardiac infarction. There was one instance of inactive rheumatic heart disease with aortic regurgitation and one of peripheral vascular disease of the Raynaud type.

In each subject the following procedures were carried out: (1) smoking, in succession, two regular cigarettes containing approximately 2 per cent of

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nicotine in the tobacco; (2) smoking two "low nicotine" cigarettes containing 0.23 per cent of nicotine*; (3) intravenous injection of 2.0 mg. nicotine bitartrate containing 0.6 mg. of the alkaloid†; (4) smoking two cubeb cigarettes containing no nicotine.‡ In a number of individuals, observations were repeated after the smoking of the regular cigarette and after the intravenous injection of nicotine.

All subjects were habitual smokers and inhaled. The regular cigarettes were of the standard commercial types and varied with the choice of the smoker. The cigarettes of low nicotine content were made from Burley tobacco naturally low in nicotine.[10] They contained approximately one-ninth as much nicotine as the standard brands. Cubebs were chosen in preference to some of the types of cigarettes free from nicotine which have been employed by other workers because they are not as irritating to the respiratory mucous membranes as are those containing ash-free filter paper and, unlike those made of corn silk, are commercially available. Furthermore, no effect on the circulation is attributed to cubeb.

The following was the routine followed. Quiet was maintained in the room in which the observations were made to avoid the occurrence of any distractions which might exert a reflex influence on the circulation. Only a single procedure was carried out on any one day. The subject rested for thirty minutes in a semirecumbent position on a comfortable hospital bed. Control readings of heart rate and of systolic and diastolic blood pressures were taken and recorded every minute for a period of ten minutes. Then two cigarettes were smoked in succession and inhaled at the patient's own chosen rate of puffing. The usual length of the smoking period was from twelve to fifteen minutes. During this period and for thirty minutes thereafter, readings of heart rate and blood pressure were continued.

The same preliminary observations were made prior to the intravenous injection of nicotine.[11] A sheet was hung before the face of the subject to obscure his view of the proceedings. Procaine was injected into the skin before the control readings were taken to avoid pain on insertion of the infusion needle. After the needle was in place, normal saline was allowed to run in slowly and after ten minutes, during which readings of heart rate and blood pressures were taken as described, 2.0 mg. of nicotine bitartrate in 3.0 c.c. of normal saline was injected through a three-way stopcock at the rate of 1.0 c.c. per minute. The subject was unaware of the shift from saline to nicotine. Observations of heart rate and blood pressures were continued for thirty minutes after the injection was completed.

For each type of stimulus, the effects were expressed as the maximal differences between the control levels and those observed after the stimulus was applied.

*Dr. H. B. Haag, Professor of Pharmacology, Medical College of Virginia, Richmond, kindly supplied the cigarettes with low nicotine content. The tobacco of commercially "denicotinized" cigarettes contains approximately 1 per cent of nicotine.

†Nicotine bitartrate in aqueous solution was supplied in ampoules by the Abbott Laboratories, through the courtesy of Dr. J. F. Biehn.

‡According to the manufacturer's label, these are composed of 80 per cent cubeb and 20 per cent inactive herbs added to obtain suitable burning qualities.

AMOUNT OF NICOTINE ABSORBED

The average American cigarette contains about 20 mg. of nicotine or 2 per cent by weight. According to Haag and Larson,[12] when a cigarette is puffed to butt length in the ordinary way, 22 per cent of the "main-stream" smoke, containing approximately 3.0 mg. of nicotine, is drawn into the mouth. In the noninhaler, from 67 to 77 per cent is absorbed.[13,14] On inhalation from 88 to 98 per cent is taken into the blood stream through the mucous membranes of the respiratory tract.[12,13,14]

Assuming 95 per cent absorption by inhalers, the amount of nicotine taken into the body from the smoke of one regular cigarette is about 2.85 milligrams. In the case of the low-nicotine cigarette, it is approximately 0.32 milligrams.* Thus, the amount absorbed from the low-nicotine cigarette was about one-ninth of that obtained from a regular cigarette and one-half as much as was injected, in terms of alkaloid, directly into the circulation.

All of the smokers remarked that both the low-nicotine cigarettes and the cubebs were unpleasant to taste and were more irritating to the mucous membranes than the regular cigarettes. Consequently, if either of these factors was responsible, in whole or in part, for inducing changes in the circulation, these should have been more pronounced when the nicotine content of the tobacco was low or when no nicotine was present. That this was not so will become clear.

RESULTS

The figures obtained were submitted to statistical analysis.† It was at once evident that there were no significant differences between the normal group and the group with cardiovascular disease, either in level of effect or in changes in that level from one type of stimulus to another. Accordingly, the results have been expressed as the combined averages of the seventeen subjects, computed by using only the first reading for those on whom the observations were repeated (Table 1).

TABLE I. COMBINED AVERAGES AND RANGES, IN SEVENTEEN SUBJECTS, OF MAXIMAL INCREASES IN HEART RATE AND BLOOD PRESSURES‡

STIMULUS	HEART RATE		SYSTOLIC		DIASTOLIC	
	AVERAGE	RANGE	AVERAGE	RANGE	AVERAGE	RANGE
Regular cigarette	15.5	4–30	14.7	8–26	11.4	6–18
Low-nicotine cigarette	9.4	0–21	8.0	0–28	5.4	0–12
Intravenous nicotine	8.5	0–32	8.0	0–25	6.0	0–19
Cubeb cigarette	3.0	4–10	3.9	0–14	2.8	0–10

‡In computing averages, the figures used for those individuals having more than one observation were only those obtained in the first series of readings.

*Personal communication from Dr. H. B. Haag, who determined the nicotine content by analysis of the smoke.

†We are indebted to Dr. John W. Fertig, Professor of Biostatistics, College of Physicians and Surgeons, Columbia University, for making the statistical analyses.

The average increase in heart rate, after the smoking of regular cigarettes, was 15.5 beats per minute; after the smoking of low-nicotine cigarettes, it was 9.4; after the intravenous injection of nicotine, it was 8.5; and after the smoking of cubebs it was 3 beats per minute.

The average rise in systolic pressure, after the smoking of regular cigarettes, was 14.7 mm. Hg; after the smoking of low-nicotine cigarettes, it was 8; after the intravenous injection of nicotine, it was 8; and after the smoking of cubebs, it was 3.9. In like sequence, the average rises in diastolic pressure were 11.4, 5.4, 6.0, and 2.8 mm. of mercury.

It is apparent that the regular cigarettes cause a significantly larger reaction, on the average, than any of the other three stimuli. The cigarettes with low nicotine content have a larger average effect than the cubebs. In the case of systolic and diastolic blood pressures, the difference between these two types of cigarettes is only of borderline significance; that is to say, it is not clearly established. The intravenous injection of nicotine produces effects not significantly different from those caused by the smoking of low-nicotine cigarettes.

By utilization of the repeat observations for regular cigarettes and for the intravenous injection of nicotine made in both this study and those published in previous papers from this laboratory,[4,11] it is possible to obtain a measure of the amount of variation within individuals. In this way, the meaning of each individual's response can be assessed. After smoking regular cigarettes, practically all individuals are reactors in the sense that the amount of change in heart rate and in systolic and diastolic blood pressures is greater than can be ascribed to chance fluctuations within the individual. After smoking the low-nicotine cigarettes or after the intravenous injection of nicotine, very few of the individuals can definitely be regarded as reactors with respect to any of the three measured effects.

By using the same measure of within-individuals variation just described it can be determined whether the individuals are significantly differentiated from each other with respect to the magnitude of the response. Only in the case of heart rate are they so differentiated, as indicated by the fact that the variation between individuals is greater than that within them. For this reason, single readings of the rise in heart rate serve to distinguish between individuals and so may be used as an index of variations in sensitivity to nicotine.

The variation within individuals, which is the basis for judging the statistical significance of each individual's reaction, is quite large. In the case of the heart rate, a change of less than 9 beats per minute could be explained as a chance fluctuation from zero. In the case of the systolic pressure the critical value is 10 mm. Hg and in the case of the diastolic it is 8. Whereas, in a statistical sense, these critical values are valid, from the clinical standpoint, sensitivity must be measured on a more conservative basis. Inasmuch as only changes in heart rate appear to differentiate between individuals in the case of the regular cigarette, and fluctuations up to 30 beats have been encountered, it is suggested, arbitrarily, that an increase of more than 25 beats per minute, after the smoking of a regular cigarette, may be regarded as a sign of hypersensitivity to nicotine. In the

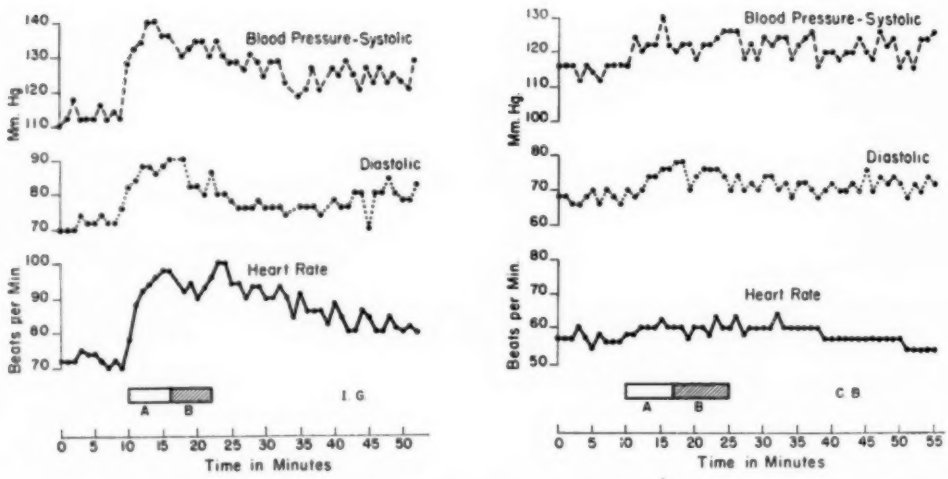

Fig. 1.—Smoking regular cigarettes. Subject I. G., 47-year-old man with coronary heart disease and anginal pain. *A*, Smoking first cigarette; *B*, second cigarette. The response is that of a hypersensitive subject. Subject C. B., 58-year-old man with no cardiovascular disease. *A*, First cigarette; *B*, second cigarette. The response is within the normal range.

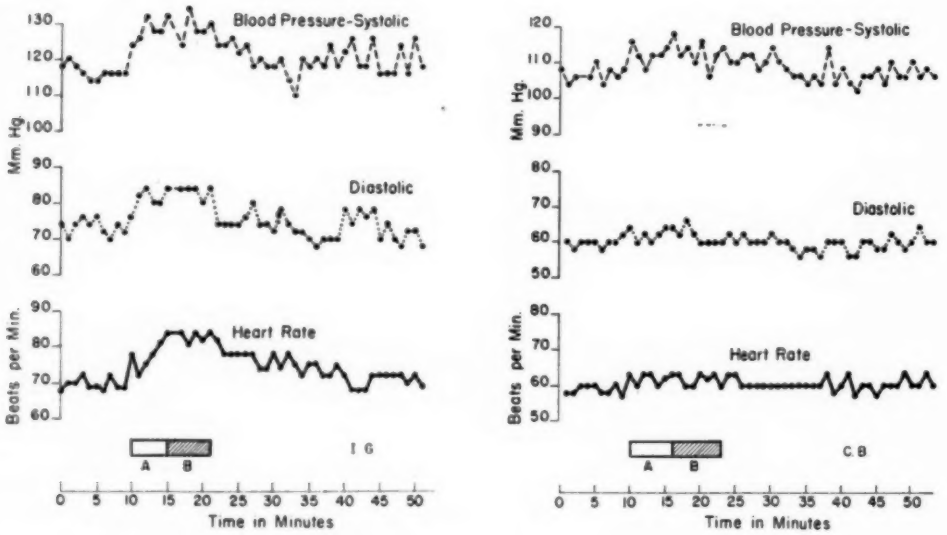

Fig. 2.—Smoking cigarettes containing 0.23 per cent nicotine. Subject I. G. *A*, First cigarette; *B*, second cigarette. Subject C. B. *A*, First cigarette; *B*, second cigarette.

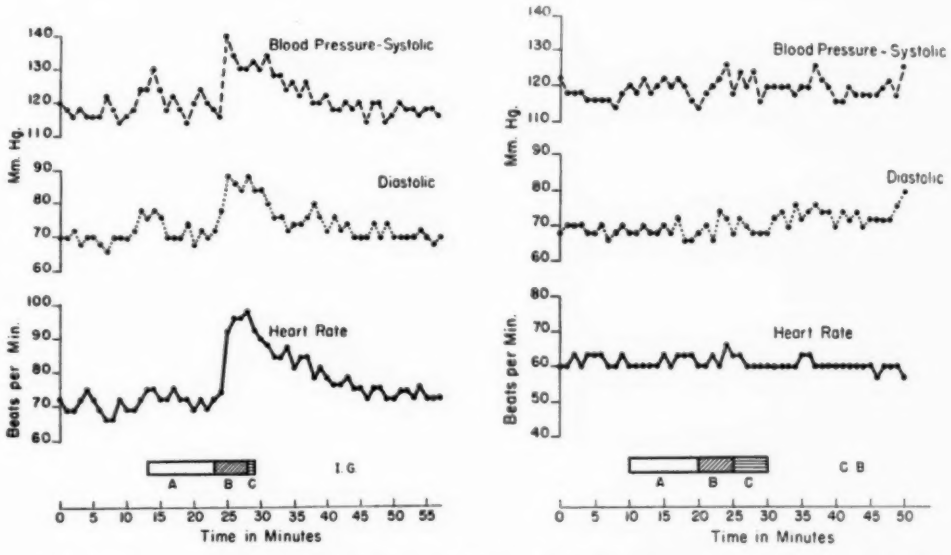

Fig. 3.—Intravenous injection of nicotine. Subject I. G. *A*, Injection of physiologic salt solution; *B*, injection of 2 mg. nicotine bitartrate; *C*, injection of salt solution. Subject C. B. *A*, Injection of physiologic salt solution; *B*, injection of 2.0 mg. nicotine bitartrate; *C*, injection of salt solution.

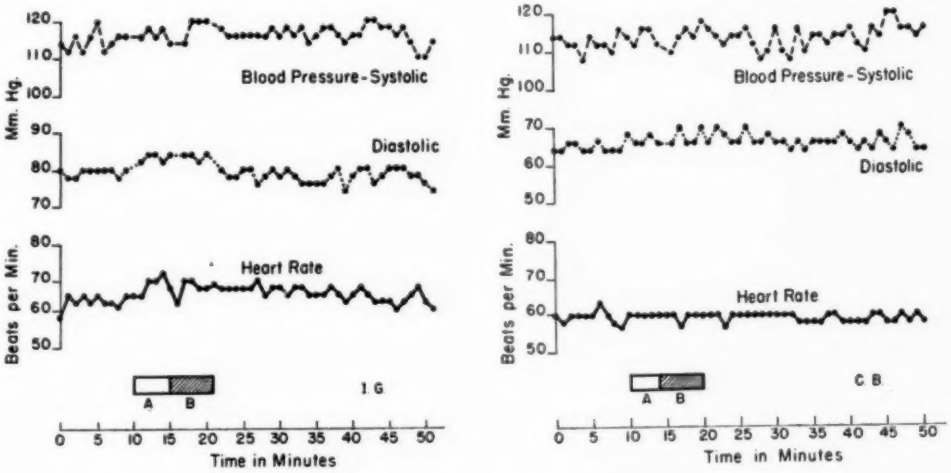

Fig. 4.—Smoking cubeb cigarettes. Subject I. G. *A*, First cubeb; *B*, second cubeb. Subject C. B. *A*, First cubeb; *B*, second cubeb.

present study, a rise of 30 beats was not exceeded in any instance, although greater increases have been reported by us in an earlier paper,[4] and by others.

Almost invariably, the maximal effects occurred after the smoking of the first cigarette; in no case, after the second, was the height of the reaction significantly increased. Within the limits of two cigarettes, therefore, there was no evidence of cumulative action.

Examples of the responses obtained to the four types of stimulus are shown graphically in Figs. 1, 2, 3, and 4, in a hypersensitive subject and in one reacting normally. The differences in levels, with respect to both stimulus and individual sensitivity, are readily apparent.

SUMMARY AND CONCLUSIONS

1. The immediate effects on the circulation of smoking regular cigarettes are due to the nicotine in the tobacco.

2. In the individual, the degree of reaction varies directly with the nicotine content of the smoke.

3. Variability in response in different persons depends to a greater extent on individual susceptibility than on the presence of cardiac disease.

4. Single measurements of the rise in systolic or in diastolic blood pressure do not serve to distinguish differences in sensitivity between individuals.

5. Acceleration of heart rate is the most sensitive index of effect. Differentiation between individuals is possible on the basis of a single reading.

6. Smoking cigarettes with nicotine content as low as 0.23 per cent, which is one-ninth of that present in the average regular cigarette, causes a significant increase in heart rate. This increase is of the same order of magnitude as that produced by the intravenous injection of 0.6 mg. of nicotine alkaloid.

7. It is suggested that, after the smoke of one regular cigarette has been inhaled, an increase in heart rate of more than 25 beats per minute may be regarded as an index of hypersensitivity to the immediate effects of nicotine.

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Abstracts

Third Inter-American Cardiological Congress

A STUDY OF DIFFERENTAL DIAGNOSIS IN AORTIC REGURGITATION.—S. Aceves, M.D., D. A. Canepa, M.D., and A. Limón Lason, M.D., Mexico, D. F., Mexico.

The material used is from the National Institute of Cardiology of Mexico. After a brief analysis of all the cases of aortic insufficiency studied in this institution and after pointing out the errors in diagnosis, the study of 143 cases of aortic insufficiency is presented. The incidence of syphilis, rheumatism, atheroma, and other causes of aortic insufficiency is given. The past history, age, sex, time of onset, clinical picture, and evolution are analyzed, together with the coincidence of subacute bacterial endocarditis and the causes of death. Special attention is paid to the importance of the diastolic murmurs at the apex. In some cases these murmurs were a decisive factor in the diagnosis, while in others they were a cause of confusion. An analysis of the electrocardiographic and roentgenographic data is made, and the elements which incline the diagnosis toward syphilis or rheumatism are pointed out. The clinical findings are compared with the findings at autopsy.

THE IMPORTANCE OF PRECORDIAL LEADS TAKEN ABOVE THE CONVENTIONAL POSITIONS IN FOLLOWING THE EVOLUTION OF MYOCARDIAL INFARCTION.—Rafael M. Alzamora, M.D., and Augusto Mispireta, M.D., Lima, Peru.

Abstract in English not available.

SOME OBSERVATIONS ON THE HUMAN ELECTROCARDIOGRAM FOLLOWING CHANGES OF ALTITUDE ENVIRONMENT.—Rafael Alzamora, M.D., and Carlos Monge M., M.D., Lima, Peru.

The electrocardiogram of man acclimatized to high altitude since prehistoric time has been studied by Monge, Saenz, Rotta, and Kerwin. Its most important characteristics are: increase in the frequency of deviation of A_{QRS} toward the right and increase of the vertical electric position of the heart. Moderate exercise resulted in inversion of the P wave, shortening of P-R, deviation of S-T, and bradycardia instead of acceleration.

We have studied electrocardiographic variations in a group of soldiers born at 10,500 feet (Huancayo), sent to 14,900 feet (Morococha) for fifteen days, and brought down to sea level (Lima).

In Morococha there was often S-T elevation and T inversion in several precordial leads. On arrival at sea level, T became normal. Further observations showed a progressive increase of QRS and T amplitude in nearly all leads, a gradual shift of the electrical axis toward the left, and a tendency for the heart to become horizontal. These modifications suggest that marked changes in the electrical activity of the heart are probably related to the physiological and chemical variations to which these soldiers were subjected. Throughout the observations the men behaved like normal subjects.

TREATMENT OF PROGRESSIVE NON-MALIGNANT HYPERTENSION IN THE OLDER AGE GROUP.—J. S. Arnason, M.D., Seattle Wash.

The results of treatment for a period of one year of eighty patients with progressive nonmalignant hypertensive disease are presented. In the group were twenty-five men and fifty-five women. The average age was 56 years for men and 62 years for women. The ages varied from 47 to 83 years. Maximum pressure recorded was 265/150, the minimum 175/90. Of these, 4 per cent showed aggravation of symptoms, with increase rather than decrease in blood pressure; 6.67 per cent showed only slight improvement; 89.37 per cent were improved. Individual and composite results are shown.

All patients without serious complications were encouraged to work since the unfavorable psychological effects of enforced idleness and the resultant continued worry was more harmful than ordinary occupation. Careful, complete examination was made and a suitable plan of treatment for each individual was worked out with special emphasis on the following: home conditions, personal habits, recreation, occupation, physical defects, diet, drugs, and frequent and continuous checkups and consultations with the physician over a period of months. Complications were briefly considered.

The results seem to compare favorably with those obtained by surgical means for this type of hypertension. The method is safer and much less expensive.

A NEW METHOD FOR THE FUNCTIONAL INVESTIGATION OF THE PERIPHERAL BLOOD-VESSELS.—Eugene Barath, M.D., Budapest, Hungary.

The functional investigation of the peripheral blood vessels plays an important role in the early diagnosis of circulatory disturbances. A new method is presented consisting in the registration of the oscillometric curves after the injection of a vasoconstrictor drug, ergotamine, 0.5 mg., and a vasodilator drug, like sodium nitrite, 0.10 Gm., dihydroergotamine, or dihydroergocornine, 0.5 milligram.

The values of the oscillometric measurements are recorded on the ordinate and the corresponding blood pressure, on the abscissa. The measurements are made on all four extremities. A decrease of the oscillatory waves after ergotamine is found in patients with increased vasospastic tone. This is often also a precursor of later coronary disease and a sign of the progressing character of the cardiovascular disease. In these patients the vasodilatation after nitrite and dihydroergocornine is often totally absent. The absence of any dilatation or constriction points to severe pathologic changes in the arterial system (torpor vascularis). Good reaction of the blood vessels with only one-sided, slight decrease of the oscillation is often a sign of beginning or benign arterial disease.

The practical importance of these methods lies in the possibility of detecting arterial and also coronary diseases in the early stage.

THE PRECOLLAGEN NETWORK OF THE HEART VALVES DURING ACTIVE RHEUMATIC FEVER.—R. Barroso-Moguel, M.D., Mexico, D. F., Mexico.

This paper deals with the role of connective fibers and undifferentiated mesenchymatous cells in rheumatic lesions of the mitral valve.

The most important findings refer to the precollagen fibrils (reticular, argyrophilic fibrils). The morphological and histochemical properties of the precollagen fibrils of the heart valves are conceived to be between those of the collagen bundles in the loose connective tissue and of the reticular network in

the hematopoietic organs. Thus, these fibrils are similar to the first fibrillar structure of the embryonal mesenchyme. When Aschoff nodules are present in the superficial verrucosities of fresh fibrin, the precollagen fibrils increase in number and in argyrophilia and penetrate into the lesions; a similar reaction is present in all nonrheumatic alterations of allergic nature. The undifferentiated mesenchymatous cells appear as polyblasts in rheumatic valvular lesions.

These results have been obtained with the techniques of silver impregnation of Rio-Hortega.

INTRACARDIAC BLOOD PRESSURE IN HUMAN SUBJECTS AND ITS RELATION TO THE RESPIRATORY PHASES.—A. Battro, M.D., H. Bidoggia, M.D., E. Pietrafesa, M.D., and F. Labourt, M.D., Buenos Aires, Argentina.

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THE EFFECT OF HYPOPOTASSEMIA ON THE ELECTROCARDIOGRAM. CORRELATION WITH CLINICAL AND CHEMICAL STUDIES.—Samuel Bellet, M.D., Carl S. Nadler, M.D., Peter Gazes, M.D., and Mary Lanning, A.B., Philadelphia, Pa.

The electrocardiographic findings in hyperpotassemia, particularly as they occur in azotemia and Addison's disease, are fairly well known. However, there are comparatively few reports on the effects of hypopotassemia. The object of this communication is to report our observations in hypopotassemia in various clinical states including the following: (a) forty-five cases of diabetic acidosis, (b) fifteen cases of vomiting due to intestinal obstruction, and (c) conditions associated with diarrhea and fluid loss.

These studies consisted of electrocardiographic and simultaneous chemical studies, including serum potassium, calcium, sodium, pH, chlorides, and carbon dioxide combining power. These patients were followed serially during their stay in the hospital. The effects of the administration of potassium and calcium in these patients were noted and correlated with the clinical, chemical, and electrocardiographic findings. The electrocardiographic alteration observed in hypopotassemia reverted to normal following the administration of potassium, and improvement in the clinical state was observed.

The role of the electrocardiogram in revealing alterations in the serum potassium is emphasized. The various patterns observed in hypopotassemia are discussed in detail. Statistical correlations were made between the potassium level and alterations in the amplitude of the T waves and Q-T segment. The implications from the standpoint of therapy in these various states are discussed.

THE VALUE OF RICE DIET IN THE TREATMENT OF ESSENTIAL ARTERIAL HYPERTENSION.—Isaac Berconsky, M.D., and Abraham Cohan, M.D., Buenos Aires, Argentina.

Rice diet was given to fifty-eight ambulatory patients with essential hypertension. The results in seventeen patients were not considered because they precociously gave up the diet, or followed it irregularly.

The changes of blood pressure in the forty-one who strictly continued the diet during 16 to 180 days are as follows: In twenty-six cases (63.4 per cent) there was a decrease from 1 to 24.5 mm. Hg in the mean arterial pressure (systolic and diastolic); in fourteen cases (34.1 per cent), a rise from 1 to 18.4 mm. Hg; and in one case there was no change. According to Kempner's criterion, we may consider three patients to have been improved (7.3 per cent) be-

cause their pressure decreased 20.5 to 24.5 mm. of mercury. These results are not of significant proportion in comparison with the results of Kempner (62 per cent) and Flipse and Flipse (62.5 per cent.) The possible objections to our results are discussed.

In a selected group of 13 cases (with urine chlorides in twenty-four hours from 0.05 to 0.48 grams), the blood pressure changes were similar to those in the forty-one cases. The slight decrease of blood pressure was ascribed to the dietary restriction of sodium.

In view of the few patients with eye-ground, electrocardiographic, and heart alterations, it was not possible to make definitive conclusions, though, in general, the observed changes were of slight significance and at times, contradictory. The same conclusion applied to subjective manifestations.

EXPERIMENTAL SURGICAL CORRECTION OF AORTIC INSUFFICIENCY.—Julio A. Berreta, M.D., and Isidro Perianes, M.D., Buenos Aires, Argentina.

A surgical aortic insufficiency was produced in dogs by means of the introduction of a valvulotome through the left subclavian artery at a place near its origin. The instrument was directed to the aortic cusps and made to perforate them thoroughly. Then there was placed in the thoracic aorta, as closely as possible to the aortic cusps, an artificial valve formed of a Vitallium tube, containing within it a cylinder of vein wall or pericardium which performed the valvular function. The tube was inserted through a hole made in the aortic wall and fixed with ligature.

We observed the disappearance or lessening of the peripheral signs of the aortic insufficiency. The dogs survived for varying periods of time. We used also two other types of valves (bullet and shovel valves) with poorer results.

THE SERUM CONCENTRATION OF A DIGITALIS GLYCOSIDE AND ITS RATE OF DISAPPEARANCE IN PATIENTS AFTER PARENTERAL DIGITALIZATION.—Rene Bine, Jr., M.D., and Meyer Friedman, M.D., San Francisco, Calif.

By employment of the embroyonic duck heart preparation, it was found possible to detect digitalis glycoside (lanatoside C) in the serum of patients given the drug and to study its rate of disappearance from that serum.

Preliminary studies had been made of the effects of (1) human blood cells and (2) serum upon the physiological activity of both the digitalis glycoside and of digitoxin. The effect of digitoxin on the embryonic duck hearts was greatly inhibited, in comparison with the very slight inhibition of the effects of the glycoside, in serum as compared with the effect in Tyrode's solution.

Quantitative determinations were made of the glycoside content of the serum of five cardiac patients who had received 1.6 mg. of lanatoside C by vein. Approximately 0.21 microgram of glycoside per cubic centimeter of serum was present in the five patients immediately after its administration. However, the average serum concentrations fell rapidly to 0.12, 0.08, and 0.06 microgram per cubic centimeter seven and one-half, fifteen, and twenty-two and one-half minutes, respectively, after injection of the drug. At the end of thirty minutes, the serum of three patients contained 0.05 microgram or less per cubic centimeter and in the remaining two patients, no glycoside was detectable in the serum. Serum samples were taken one, two, twelve, and twenty-four hours after injection of the glycoside, but none contained detectable glycoside.

OBSERVATIONS ON FATTY INFILTRATION OF THE MYOCARDIUM.—WILLIAM A. BRAMS, M.D., and KURT BISS, M.D., CHICAGO, ILL.

It has not yet been established that fatty infiltration of the myocardium can result in significant clinical manifestations or that it may lead to serious consequences. The literature pays scant attention to this subject and most modern textbooks on cardiology dismiss it with few words.

Significant fatty infiltration occurred in 6 per cent of adults among 5,831 autopsies. The right ventricle was involved alone or predominantly in 90 per cent and both ventricles equally, in 10 per cent; there was no instance of isolated left ventricular involvement. Body weight was not a factor, but fatty hearts were present in the majority of patients who had diabetes, gall bladder disease, or disease of the liver or pancreas. Seven cases with sudden death are reported: two patients had congestive failure, and one had paroxysmal tachycardia; death was unexpected in four others. Patients with fat-infiltrated hearts withstand surgery poorly; there is a tendency to sudden death. No distinctive clinical manifestations occur. It apparently simulates other forms of diffuse myocardial disease.

The object of this report is to awaken interest in the subject so that more material and further study might lead to the establishment of a clinical picture.

CHANGES IN THE FRONTAL AND SAGITTAL ELECTROCARDIOGRAM OF HYPERTENSIVE SUBJECTS DURING AN EXPERIMENTALLY PRODUCED PHASE OF LOWERED BLOOD PRESSURE.—J. BRUMLIK, M.D., and C. E. KOSSMANN, M.D., NEW YORK, N. Y.

Regression of changes in the so-called "typical electrocardiogram" of essential hypertension, sometimes occurring spontaneously or as observed after the use of nitrites, potassium salts, and lumbar sympathectomy, have attracted considerable attention. Because of the clinical importance attached to this phenomenon, especially after treatment, an attempt was made to produce it by another method.

A temporary reduction of blood pressure was obtained in fifteen patients with essential hypertension by the intravenous administration of typhoid vaccine. The usually associated rise in temperature was partly or completely eliminated by premedication with aminopyrine. During the period of lowered blood pressure the changes observed in standard and special electrocardiographic leads (including the sagittal leads of Arrighi) can be summarized as follows:

The mean electrical axis of QRS and of QRS-T was deviated slightly to the right or was not affected at all. Variations in the order of ventricular repolarization caused a decrease in positivity or an increase in negativity of the T wave chiefly in Lead I. Similar changes were sometimes observed in certain of the sagittal leads only.

Conclusion.—The observed electrocardiographic changes demonstrate that a sudden and transient fall in blood pressure induced by intravenous pyrogen does not make the "hypertensive electrocardiogram" assume a more "normal" appearance, but, on the contrary, makes it assume a more abnormal configuration.

PENETRATING WOUNDS OF THE HEART. CLINICAL, RADIOLOGICAL AND ELECTROCARDIOGRAPHICAL STUDY. — FRANK CANOSA LORENZO, M.D., HAVANA, CUBA.

We have studied from a clinical, radiological, and electrocardiographical point of view, patients presenting penetrating wounds in the heart caused by knife or bullet. Exclusively pericardial lesions are not included in this report.

Most of the patients had parietal wounds which only touched the muscle. In two patients the wound entered a cavity of the heart. In a patient wounded by a bullet, a free passage between the pericardium, pleural cavity, and the exterior was established with considerable hemorrhage. In four cases a rapid accumulation of blood in the pericardiac cavity produced the syndrome of acute cardiac compression. A hemopericardium appeared slowly in one patient causing chronic heart tamponade.

In all of these pateints paracentesis of the pericardium was performed, not only as a diagnostic method but for treatment. The radiological examination in this series was useful and interesting. The electrocardiogram gives us knowledge of involvement of the heart. The use of the multiple unipolar precordial leads in our study shows great superiority over the use of only a single precordial lead for the diagnosis of the myocardial lesion and its location.

UPPER ABDOMINAL PAIN AND ANGINA PECTORIS. — GEORGE D. CAPACCIO, M.D., SEATTLE, WASH.

Factors concerned with anginal pain, coronary sclerosis, and upper abdominal disorders, such as gallbladder disease, chronic peptic ulcer, and other conditions, are discussed. An attempt is made to clarify the interrelationship of this controversial subject. The altered coronary blood flow from reflex change is accepted but the added feature in the production of anginal pain is the supposition that upper abdominal pain acts *also* in the same capacity as overexertion or excitement in initiating an anginal episode.

A representative case is reported of a woman of 60 years with coronary sclerosis, angina pectoris, and pain in the upper abdomen due to a penetrating, stenosing, duodenal ulcer. A subtotal gastric resection and partial duodenectomy was performed which was followed by an uneventful convalescence, immediate disappearance of all pain, and subsequent absence of both types of distress on a moderately restricted regime.

It is the opinion of the author that the severe pain of the ulcer acted not unlike overexertion in imposing an additional load upon a heart already affected by coronary sclerosis. This symptom complex of pain in the upper abdomen followed by anginal distress was interrupted by surgery.

THE DIAGNOSIS OF SEPTAL DEFECTS BY MEANS OF THE LEVO-ANGIOCARDIOGRAM.—AGUSTIN CASTELLANOS, M.D., HAVANA, CUBA.

Some authors believe that angiocardiography has no value as an aid in the diagnosis of interauricular and interventricular communications.

Some years ago, we published an article pointing out the direct and indirect signs obtained by means of dextroangiocardiograms in Roger's disease. In cases of interauricular communication the following dextroangiocardiographic images are obtained: (1) When the septal defect is small, opacification occurrs only at the left auricle. In such a case the normally clear space between the lower end of the superior vena cava and the pulmonary artery trunk, in anteroposterior position, disappears, and it is seen to be quite opaque. (2) When the septal defect is large, there is a total radio-opacification of the heart (cast-image).

It is true that in some cases of septal defects we may obtain a normal dextroangiocardiogram; and that is the reason why some years ago we applied the levoangiocardiogram, which is always of great value, because in such types of defect the blood pressure at the left cavities is higher than that in the right cavities, and the opaque material passes from left to right. In a normal levoangiocardiogram, no opaque material appears within the right cavities and the

pulmonary artery. In cases of interauricular communication, there is radio-opacification of the left cavities and aorta, and also of right auricle and ventricle. In cases of interventricular communication, besides the left cavities and aorta, there is opacification of the right ventricle and the pulmonary artery. The method is useful for getting an idea of the size of the septal defect. If the septal defect is very large, the pulmonary artery is more opaque than the aorta. If there is a small defect, the reverse is true.

The differential diagnosis between interauricular and interventricular communication consists in the radio-opacification of the right auricle, which occurs in cases of interauricular defect, whereas in cases of interventricular defect there is no radio-opacification of the right auricle. In this fact lies the importance of the oblique positions.

DYNAMIC MODIFICATIONS OF THE RIGHT VENTRICLE ANGIOCARDIOGRAPHICALLY STUDIED.—Alejandro Celis, M.D., Enrique Arce Gomez, M.D., and H. Castillo, M.D., Mexico, D.F., Mexico.

The paper describes the technique used by one of us (A. Celis) for the purpose of obtaining the exclusive angiocardiographic picture of the right ventricle. The triangular form of the diastolic picture in the postero-anterior position is discussed. Its borders are described and its relations to those of the cardiovascular silhouette are pointed out. The dynamic modifications of the right ventricle during its contraction are studied. The picture of the right ventricle in the left transverse position and its dynamic alterations are analyzed. The presence of a residual opaque substance (incomplete emptying of the right ventricle) is mentioned. The described modifications are discussed.

SALICYLATES. NEW PHARMACOLOGICAL ASPECTS WITH A VIEW TO THEIR USE IN RHEUMATIC FEVER.—Teodoro E. Cesarman, M.D., and Salvador Martín, Q.F.B., Mexico, D.F., Mexico.

This study attempts to demonstrate that the beneficial effects of sodium salicylate and acetylsalicylic acid are products of slow elimination. It is based on work done with rheumatic fever patients of the National Cardiological Institute of Mexico and with healthy individuals.

A new method of estimating the salicylate content in the blood is used. The exactness of the method is demonstrated and a comparison is established between it and the one used by Coburn. Sodium salicylate and acetylsalicylic acid administered every twelve hours were capable of producing, in a short time, a sustained blood level. The drug was administered in doses of 0.10 Gm. per kilogram of body weight in twenty-four hours (two doses of 0.05 Gm. per kilogram every twelve hours) and the concentrations obtained ranged between 332 and 561 gamma. Higher concentrations were obtained when the doses were administered twice every twenty-four hours than when the salicylates were given in six or eight divided doses. On the administration of moderate quantities of alkali, no important modification in the blood concentration of salicylates was noticeable.

A preliminary report is made on the role played by the hematocrit in the blood concentrations of salicylate and some other products.

SURGICAL TREATMENT OF HYPERTENSIVE HEART DISEASE AND OF HEART FAILURE OF HYPERTENSION.—Ignacio Chávez, M.D., and Luis Méndez, M.D., Mexico, D.F., Mexico.

Published in full in this issue.

TREATMENT OF PERIPHERAL VASCULAR DISORDERS BY TRANSFER OF IONS OF MECHOLYL.—NICANDRO CHÁVEZ, M.D., MEXICO, D.F., MEXICO.

Three thousand one hundred five treatments were given to 103 patients. In every case, oscillometric readings and the temperature at the distal end of the fingers were taken before, just after, and two hours after treatment. Mecholyl solutions were used at different concentrations until toxic symptoms developed with high dosage. The optimum concentration was 1 per cent. With this dose, gradual and increasing temperature and oscillometric curves were observed. In cases of organic occlusion these findings do not change. On the other hand, the collateral circulation improves considerably. The treatment can be given daily, for long periods of time with absolute tolerance by the patient.

THE UNIPOLAR LEADS OF THE ELECTROCARDIOGRAM IN RIGHT VENTRICULAR ENLARGEMENT.—JUAN CODINA-ALTÉS, M.D., and CARLOS PIJEAN DE BERISTAIN, M.D., BARCELONA, SPAIN.

The electrocardiographic changes observed in right ventricular enlargement are probably due to two distinct factors: (1) increase in thickness of the right ventricular wall and (2) changes in the position of the heart. The characteristic change of the hypertrophy is the increased amplitude of the R wave and diminution of the S wave in the right thoracic leads. This may lead to a complete disappearance of S and the presence of a high R wave, which may be preceded by a small Q wave. Changes in the position of the heart are manifested by a deep S wave in the left thoracic leads. In these, the QRS group may become predominantly negative. The same position changes account for the late positivity of aV_R and for the fact that aV_L becomes deeply negative. When the heart enlargement is only slight or moderate, aV_F resembles the left thoracic leads. When the hypertrophy extends itself to the inflow tract of the right ventricle, the potential variations originating in this chamber are transmitted not only to the right side of the precordium but also to the left leg, and aV_F resembles V_1 and V_2.

The RS-T and T-wave changes are not, as a rule, important. In lead V_6, T is always positive and in aV_R, always negative.

THE UNIPOLAR LEADS OF THE ELECTROCARDIOGRAM IN LEFT VENTRICULAR ENLARGEMENT.—JUAN CODINA-ALTÉS, M.D., and CARLOS PIJEAN DE BERISTAIN, M.D., BARCELONA, SPAIN.

The characteristic modifications of the unipolar leads of the electrocardiogram in left ventricular enlargement are: (1) increased negativity of the right thoracic leads, (2) increased positivity of the left thoracic leads, (3) sudden shift between the QRS groups registered at the right side of the precordium and those obtained at the left side, (4) displacement to the left of the point at which the highest R wave may be registered, (5) possibility of a higher R wave in Lead V_6 than in V_4, and (6) increased amplitude of the QRS group. A Q wave is often registered in the left positions, a useful point in differentiating left bundle branch block.

Because of changes in the position of the heart, Lead aV_L resembles the left thoracic leads and aV_F the right ones. This is traduced in the standard leads by a "left axis deviation." These position changes are not always present and the heart may remain in a more or less vertical situation. In these cases, nevertheless, the thoracic leads show the same typical changes.

The RS-T segment tends to become elevated in Leads V_1, V_2, and aV_R and depressed in V_4, V_5, V_6, and aV_L. In the first of these leads, T tends to be positive and in the second ones, negative.

THE ENDOCARDIAL ELECTROCARDIOGRAM UNDER PATHOLOGICAL CONDITIONS OF THE PERICARDIUM AND OF THE MYOCARDIUM.—E. Coelho, M.D., J. M. Fonseca, M.D., and Adelaide Constantino, M.D., Lisbon, Portugal.

The intracavity potential of the dog in certain experimental conditions was studied with the unipolar derivations. The electrodes were introduced in the right cavities through the jugular vein, and in the left ventricle, through the carotid artery. The procedure consisted in altering the pericardial surface, provoking in some experiments generalized pericarditis and in others partial necrosis of the wall, without reaching the endocardium. In pericarditis as well as in the partial necrosis of the wall of the heart (always with pericarditis epistenocardica), the fundamental alterations of the electrocardiogram consisted in depression of RS-T segment, more or less intense, and deep negativity of the T wave. Lengthening of QS in the final period of the experiment was also observed. We could not obtain characteristic records of localization, except when we interfered with the posterior wall and reached the septum (producing lesions of the bundle of His). The electrocardiographic alterations of the two series of experiments were studied immediately and some days after the operation.

EXPERIMENTALLY PRODUCED CORONARY ARTERY INSUFFICIENCY, CORONARY ARTERY SPASM, AND A DEMONSTRATION OF THE REMARKABLE RESERVE POWER OF THE HEART.—Eliot Corday, M.D., Ramon Spritzler, M.D., H. C. Bergman, Ph.D., H. E. Krueger, M.D., and Myron Prinzmetal, M.D., Los Angeles, Calif.

This subject is discussed in this issue.

SURGICAL TREATMENT OF THE CARDIAC LUNG.—P. Cossio, M.D., and I. Perianes, M.D., Buenos Aires, Argentina.

After emphasizing the importance of the cardiac lung in clinical heart disease, the authors conceived the possibility of the surgical control of the lung engorgement by left ventricular failure or mitral stenosis, when the condition cannot be controlled by the classical medical treatment.

With this object several surgical procedures on dogs were performed, some of them designed to drain the lungs (anastomosis of pulmonary veins and other vessels of the systemic circuit) and others to reduce the output of the right ventricle (tricuspid insufficiency produced by valvulotomy through the internal jugular vein with an instrument which also permits the measurement of the intracardiac pressure and ligation of the inferior vena cava below the renal veins, according to the retroperitoneal technique in use).

Once the technique was developed and assurance obtained that human subjects could tolerate both procedures, first one and then the other, or only one, were practiced with success on patients with severe heart failure not controlled by medical management. The dyspnea decreased and the patients could sleep the whole night in the supine position, whereas before they had had to remain seated. The physical capacity also increased, the patients being able to walk without difficulty. This improvement continued for six months after the tricuspid valvulotomy. The ligation of the inferior vena cava caused total disappearance of the rise of the venous pressure following the elevation of the lower limbs. The surgical treatment of the cardiac lung does not attempt to cure this condition definitely; it only attempts to lengthen the life with fewer limitations and without too much discomfort.

MORPHOLOGICAL EVIDENCE OF SPECIFIC INFLAMMATION IN THE BRAIN OF RHEUMATIC PATIENTS.—I. Costero, M.D., Mexico, D.F., Mexico.

The histologic changes which are always present in the brain of patients with active rheumatic fever are localized in the capillary vessels and in the microglial cells. Such changes will be described in detail.

In the brain of some children dying of active rheumatic fever, I have found certain nodules of ramifying microglia, which begin in miliary foci of necrobiosis localized most commonly in the gray matter of the pons. The Hortega cells of these nodules soon undergo clasmatodendrosis and give place to small areas of demyelinization, in which a few large neuroglia cells of the protoplasmatic type are found. The nodules are not necessarily related either to the blood vessels or to any of the other lesions, and they disappear within a short time without leaving a detectable connective-vascular scar.

It is possible that the nodules of ramifying microglia represent a hyperergic reaction similar to that responsible for the Aschoff nodule in connective tissue. They may, therefore, be useful for the histopathologic diagnosis of the encephalitic lesions during the evolutive period of rheumatic fever.

EXPERIMENTAL STUDIES ON THE VALIDITY OF THE CENTRAL TERMINAL OF WILSON AS AN INDIFFERENT REFERENCE POINT.—Martin Dolgin, M.D., Sidney Grau, M.D., and Louis N. Katz, M.D., Chicago, Ill.

To be published in full in the *American Heart Journal*.

COMMON SENSE MANAGEMENT OF AMBULATORY CORONARY ARTERY DISEASE.—Maurice A. Donovan, M.D., Schnectady, N. Y.

This paper discusses the genral management of ambulatory coronary disease in a series of eighty-nine patients observed over a two- to five-year period. It emphasizes the value of proper nitroglycerine therapy, the dietary management of obesity and high blood cholesterol, and a low sodium intake in associated hypertension. It emphasizes the worth of a proper psychosomatic evaluation in each patient. This necessitates a detailed personal history wherein the social, economic, and emotional problems of the individual are carefully considered. It often entails a painstaking investigation of the effect of their reactions upon the general attitude of the patient. When diagnosis has been obscure, a complete differential diagnostic workup has proved most valuable. It clearly shows the necessity for allotting ample time in each instance for frank discussion of the pathological problems involved. Some of these ambulatory patients have had former acute myocardial infarctions, but the majority fall into the clinical syndrome of coronary insufficiency.

THE RIGHT HEART CAVITIES, THE PULMONARY ARTERY AND THE INTERVENTRICULAR SEPTUM, FROM THE ANGIOCARDIOGRAPHIC VIEWPOINT.—Narno Dorbecker, M.D., and Jorge Deschampa, M.D., Mexico, D.F., Mexico.

The material used for this study has been selected from 265 angiocardiographic tracings made by the authors in the National Cardiological Institute of Mexico. Studies made preferably, but not exclusively, in cases of congenital heart disease, include: persistence of the ductus Botalli, interauricular septal defect, persistence of the common atrioventricular ostium, common arterial trunk, tetralogy of Fallot, complex of Eisenmenger, tricuspid atresia, and so forth.

The location, size, form of filling, time of emptying, interrelations, and distribution of the opaque substance have been studied, and the results compared with the data obtained from simple radiological studies. The similarities and differences shown in specific pathological states have been noted and the findings which may serve for differential diagnosis are pointed out. The position of the interventricular septum and the variations it undergoes in various abnormal states are indicated. The position, size, and relations of the pulmonary artery under abnormal conditions and its radiographic appearance in simple studies are demonstrated.

THE ELECTROCARDIOGRAM IN CASES OF VENTRICULAR ANEURYSM.—Maurice Eliaser, Jr., M.D., San Francisco, Calif.

The electrocardiographic changes in cases of ventricular aneurysm following myocardial infarction of the left ventricle have been reviewed. Records of previously published authentic cases and a personally observed series of fifteen instances have been classified. No pathognomonic electrocardiographic patterns have been detected, but two types of records have been observed to have occurred sufficiently frequently to be of clinical significance. In 37.7 per cent of cases the standard electrocardiograms reveal a downward directed major deflection in Lead 1, usually with inversion of the T wave and an upright P wave, with a positive ventricular complex in Lead III (QS_1 type). In 31.1 per cent of cases the ventricular complex in Leads II and III are directed downward with an upright major deflection in Lead I that may or may not be of low amplitude ($S_{2,3}$ type). In the remaining cases 13.3 per cent and 17.8 per cent reveal bundle branch block and nonspecific changes associated with myocardial infarction, respectively. Unipolar electrocardiography reveals that the QS_1 and $S_{2,3}$ types of record are caused by superimposition of rotational changes of the heart on patterns associated with myocardial infarction of the left ventricle. The initial position of the heart and the subsequent location of the aneurysmal sac are major factors in determining the ultimate configuration.

PRIMARY HEALED BACTERIAL VALVULAR ENDOCARDITIS WITH MULTIPLE MYOCARDIAL INFARCTS.—Norbert Enzer, M.D., Milwaukee, Wis.

This presentation is concerned with the detailed clinical and post-mortem records of a man who presented during life many of the features of subacute bacterial endocarditis. At no time during this illness was the diagnosis established by blood cultures. Post-mortem examination revealed the presence of a healed mitral endocarditis and multiple infarcts in the myocardium. In certain areas of the myocardium close to the endocardium, bacteria were identified in the sections. Nowhere in the tissues was there any evidence of rheumatic fever or other antecedent myocardial or endocardial disease. The diagnosis is further supported by the demonstration of renal lesions and multiple peripheral vascular lesions. The case further illustrates the importance of mural endocarditis which is active, while the valvular endocarditis is demonstrably healed.

THE FACTOR OF PULMONARY EMPHYSEMA AND RIGHT HEART STRAIN IN UNCOMPLICATED PULMONARY FIBROSIS (PNEUMOCONIOSIS).—Norbert Enzer, M.D., Milwaukee, Wis.

The pneumoconioses, especially silicosis, have attracted a great deal of attention and study in the past fifty years. These studies have been largely devoted toward a solution of the problems involved in the etiology and mechanism of the fibrosis. The high coincidence of tuberculosis stimulated research in that direction, too.

Only more recently has attention been directed to the effects of fibrosis on the nontuberculous lung. Investigations in this direction call for an appreciation of the pathogenesis and behavior of pulmonary emphysema, pulmonary arteriosclerosis, chronic bronchitis, bronchiolitis, fixation of the hilum, and the effect of all of these singly and combined on pulmonary ventilation, pulmonary circulation, and the functions of the right heart. This complex has an important clinical aspect, for it is involved with the evaluation of these patients in terms of disability. Such disability sometimes is of great importance because of the Workmen's Compensation Law.

This presentation is concerned with the development of clinical, physiologic, and pathologic evidence aligned to throw some light upon the symptom complex of pulmonary fibrosis. Cases illustrating various phases will be used to highlight the thesis that, "Simple nodular, uninfected pulmonary fibrosis may be the cause of severe pulmonary emphysema, and that patients so affected are disabled because of this, and frequently die of right heart failure."

ORGANIC HEART DISEASE IN MALTA FEVER.—J. C. Etchevés, M.D., A. Cozza, M.D., and A. Alfonsín, M.D., Buenos Aires, Argentina.

Abstract in English not available.

THE ELECTROCARDIOGRAM IN PNEUMOPERITONEUM INCLUDING AUGMENTED UNIPOLAR LIMB LEADS AND UNIPOLAR CHEST AND ESOPHAGEAL LEADS.—Elwyn Evans, M.D., and Thomas C. Black, M.D., Orlando, Fla.

New terminology to facilitate description of the location of the chest electrode in positions other than C_1 through C_7, etc., was used. Positions starting one intercostal space above C_1 were labeled C', positions starting two intercostal spaces above were labelled C'', and those three intercostal spaces above, C'''. Those one intercostal space below were marked $C\text{-}'$. Positions on the right were further identified by R.

Pneumoperitoneum changed all records in various degrees, but the changes were not always predictable. Esophageal tracings were taken on ten patients with pneumoperitoneum (four with left and three with right phreniphraxis). Three were taken with patients erect, seven erect and recumbent, and one during various phases of respiration. At ventricular levels, all showed abnormally large Q waves; nine showed abnormal T waves. Other constant findings were upward and probably forward displacement of the heart, noted roentgenographically.

It is concluded that heart position affects the electrocardiogram, including esophageal leads. Further, it is hazardous to diagnose old posterior myocardial infarction from the history when it is substantiated only by abnormal esophageal electrocardiograms.

CARDIAC OUTPUT IN ACUTE HYPOXEMIA.—M. Feldman, Jr., M.D., S. Rodbard, Ph.D., and L. N. Katz, M.D., Chicago, Ill.

This laboratory has recently been engaged in an analysis of the hemodynamic changes which occur after the induction of 100 per cent nitrogen breathing in anesthetized dogs. Immediately after the onset of nitrogen breathing, the blood flow nearly doubles in the superior vena cava, with a lesser increase in the inferior vena cava. Within seventy seconds a rise of blood pressure of 10 to 40 mm. Hg is observed. After the blood pressure begins to fall from its peak value, and when it has almost returned to its control value at about one hundred seconds, the flow in the inferior vena cava suddenly falls to nearly zero, although the flow in the superior vena cava also diminishes. With the resumption of air

breathing, there is a rapid return of flow in both the superior and inferior venae cavae, concomitant with a marked rise in blood pressure. After about three to four minutes the pressure and flow return to control values. The implications of these data are discussed.

BIOMETRIC PROFILE OF HYPERTENSIVE PATIENTS AT BOGOTA.—Luis G. Forero Nougues, M.D., Bogota, Colombia.

At Bogota, Colombia, situated at an altitude of 2,615.215 meters above sea level, with a barometric pressure of 560,138 mm. Hg ± 0.834, three hundred forty-three hypertensive patients were studied biometrically according to the criteria of the New York Heart Association. Of these, 207 were women and 136 were men.

The findings were treated statistically with the following results:

Female Patients			Male Patients		
Weight	62.290 kg.	± 9.982	Weight	74.379 kg.	± 9.3882
Age	51.866 yr.	± 9.712	Age	53.755 yr.	± 8.6263
Electrical axis	+30°	± 4.599	Electrical axis	+30°	± 4.378
Height	155.50 cm.	± 5.254	Height	168.9 cm.	± 5.963
Vital capacity	2,269.0 c.c.	± 4.920	Vital capacity	3,168.4 c.c.	± 6.1068
Pulse	79.55 per min.	± 3.208	Pulse	74.20 per min.	± 3.386
Systolic blood pressure	17.30 cm. Hg	± 2.972	Systolic blood pressure	16.522 cm. Hg	± 2.7265
Nonprotein nitrogen	36.108 mg. %	± 1.519	Nonprotein nitrogen	38.821 mg. %	± 1.732
Distance between midsternal line and heart apex	97.049 mm.	± 1.753	Distance between midsternal line and heart apex	107.62 cm.	± 1.900
Diastolic blood pressure	9.827 cm. Hg	± 1.586	Diastolic blood pressure	9.7613 cm. Hg	± 1.6751
Respiration	20.18 per min.	± 1.41	Respiration	20.238 per min.	± 1.536
Surface area	1.607 sq. M.	± 0.884	Surface area	1.810 sq. M.	± 0.7964
Intercostal space	5.366	± 0.7312	Intercostal space	5.395	± 0.7174
Optic fundus	1.652 (K-W grouping)	± 0.715	Optic fundus	1.7594 (K-W grouping)	± 0.7947

RÉSUMÉ OF PRESENT CONCEPTIONS OF HYPERTENSION.—Salvador García Tellez, M.D., Mexico, D.F., Mexico.

Abstract in English not available.

BIOSYNTHESIS OF RADIOACTIVE DIGITOXIN USING CARBON 14.—E. M. K. Geiling, M.D., F. E. Kelsey, M.D., and B. J. McIntosh, M.D., Chicago, Ill.

The availability of carbon 14 now makes possible the preparation of a large number of important drugs with reasonable amounts of radioactivity incorporated in the molecule either by direct chemical synthesis or by biosynthesis. We have prepared radioactive digitoxin from the dried leaves of Digitalis purpurea grown in the laboratory.

Suitable young plants were transplanted into quartz sand and maintained with an inorganic nutrient solution. Each plant was sealed in two battery jars placed with the open ends in apposition. Carbon 14 was introduced as carbon dioxide. The sealed plants grew well and were harvested after about thirty days of exposure to C14.

Radioactive digitoxin was extracted from the dried leaves with 50 per cent alcohol. The extract was purified by precipitation with lead acetate; the digitoxin was removed with choloroform and precipitated from dilute alcohol solution. Determination of radioactivity was made by using nonradioactive digitoxin as a carrier, with a mica-window Geiger counter.

The activity of the preparation is such that approximately 5 per cent of the total dose in animals can be detected with accuracy. Tissue distribution studies in isolated heart preparations as well as in small laboratory animals are now under way.

IMPORTANCE OF PSYCHIC COMPONENTS OF PAIN IN THE COURSE OF CORONARY DISEASES.—R. GODEL, M.D., ISMAILIA, EGYPT.

In coronary diseases, whether the latter causes transitory myocardial ischemia or subacute infarction, pain of purely psychic origin frequently adds its component to the syndrome. Should such pain be severe, occur repeatedly, and be associated with anxiety, then the clinical picture becomes greatly confused. The origin of each single crisis is erroneously traced back to coronary insufficiency; prolonged bed rest is enforced upon the patient who becomes ever more heart-conscious, distressed, and emotionally fixed upon his ailment.

However, before the psychic components of the pain are searched for, the patient should undergo thorough cardiological investigation. The type of coronary disease which affects him is determined: chronic nonprogressive form, progressive type, or protracted coronary insufficiency. This task rests upon careful interpretation of clinical signs and symptoms, serial electrocardiograms, blood sedimentation figures, and leucocyte counts. Psychic components are then analyzed and their relative importance estimated. The patient should be encouraged and helped to work out his emotional problems. These may have centered upon sexual, competitive, aggressive forces, and upon relationships of a more or less regressive type. Narcoanalysis can help in liberating repressed complexes and conditionings. Elimination or attenuation of disturbing psychic material will considerably reduce the frequency of cardiac pain. It will also help clarify the clinical picture.

AN OPTIMAL SYSTEM FOR THE TREATMENT OF THE FAILING HEART.—HARRY GOLD, M.D., NEW YORK, N. Y.

The conclusions of extensive experience are presented.

A SIMPLE METHOD OF DETERMINING ABNORMALITIES OF THE Q-T INTERVAL AND ITS VALUE IN ACUTE RHEUMATIC FEVER.—EMANUEL GOLDBERGER, M.D., AND MURRAY J. POKRESS, M.D., NEW YORK, N. Y.

To be published in full in *American Heart Journal*.

CONTRIBUTION TO THE STUDY OF ERYTHROBLASTEMIA IN CARDIAC PATIENTS.—I. GONZALEZ GUZMAN, M.D., MEXICO, D.F., MEXICO.

Studying several thousands of cytohematic examinations made at the National Institute of Cardiology of Mexico, we found some showing a significant percentage of erythroblasts in the blood. The analysis of the corresponding clinical data revealed some important facts, which can be summarized as follows:

1. Anemia of about 2.0 million red cells per cubic millimeter generally shows some circulating erythroblasts. This erythroblastemia is always slight; it is not constant and has no relation to the number of red cells.

2. When anemia appears together with cardiac failure, the erythroblastemia is more frequent and important; it is not related to the anemia, but to the degree of cardiac failure.

3. In cases of marked heart failure erythroblasts appear in the blood sometimes in high percentages even when the number of red cells is normal or above normal.

4. The nucleated red corpuscles present in cases of heart failure are all normoblastic, seldom basophilic, and almost always polychromatic and orthochromatic.

5. In cases of cardiac failure with pulmonary infarct, bronchopneumonic foci, or pneumonia, binucleated normoblasts, paraerythroblasts of Lehndorff, appear in the circulation.

6. The significance of paraerythroblasts is discussed and some experiments on their origin are outlined. The clinical and experimental data lead us to conclude that the normoblastic nuclei suffer a deformation and the normoblasts take on a binucleated appearance because of colloidal conflicts of the antigen-antibody type which take place in the interior of nucleated corpuscles. The antigens are degraded proteins liberated in tissues in which an extravasation of red corpuscles occurs. The antibodies are elaborated by the organism as a response to the degraded proteins which are set free from the red cells when they are destroyed in a tissue rich in reticuloendothelial cells.

7. The cause of erythroblastemia is anoxia of the bone marrow.

PATTERN Q_1-Q_2-Q_3. ROTATION AND DISPLACEMENT OVER THE THREE EXPERIMENTAL AXES.—Antonio Gómez Hernández, M.D., Havana, Cuba.

The technique for rotating and displacing the heart on its three axes to extreme positions is described. It is confirmed that by clockwise rotation of the heart, the S_1 Q_3 pattern is always obtained, and by counterclockwise rotation, Q_1 S_3 is produced. Likewise, convergent tracings are produced in V_L and V_F by making the heart vertical, that is, moving the apex to the right. On the other hand, divergent tracings are produced by making the heart horizontal by moving the apex to the left. On backward projection of the apex the pattern S_1 S_2 S_3 described by Ashman is produced. This does not occur when the apex is moved forward. It is necessary to rotate the heart a little clockwise in order to cause the initial negative element Q to be produced without exception. Five cases are shown of the Q_1 Q_2 Q_3 pattern, two of them with amplitudes and widths above the values considered as normal. Aside from this, we were not able to obtain in these cases clinical or radiographical evidence of cardiovascular pathology.

MERCURIAL DIURETICS. A NEW THERAPEUTIC APPROACH WHEN INTOLERANCE OR HYPERSENSITIVITY EXISTS.—Luis González Sabathié, M.D., V. S. Terán, M.D., and O. Robiolo, M.D., Rosario, Argentina.

Abstract in English not available.

PAROXYSMAL TACHYCARDIA OF INFANTS UNDER ONE YEAR.—Luis González Sabathié, M.D., and Osvaldo Robiolo, M.D., Rosario, Argentina.

Eight observations of paroxysmal tachycardia of infants under one year are reported. These, in addition to the forty-three observations found in the literature, bring the number of reports on this rare clinical phenomenon to fifty-one. These cases were studied between 1938 and 1946, five of the cases having occurred in the same year. All were of the supraventricular type. Six cases ended in recovery, two in death.

The clinical picture is described in detail. Symptomatology, duration of the attacks, their repetition, maternal antecedents, existence of etiological factors, immediate and later evolution, type of tachycardia, and noticed frequency are analyzed. The electrocardiograms are analyzed, and the modifications after the end of the attack pointed out. They appear as a true post-tachycardial syndrome caused to a large extent by the use of quinidine.

For the cases observed during pregnancy, it is proposed to use the term "Prenatal Paroxysmal Tachycardia," instead of "Congenital Paroxysmal Tachycardia."

The therapeutic remedies used to date are discussed, and the form is described in which quinidine sulfate has been used orally with good results and without untoward effects.

The mechanical procedure of vagal stimulation gave good results in two cases observed.

CALCIFICATION OF THE MYOCARDIUM.—Luis González Sabathié, M.D., and M. Voogl, M.D., Rosario, Argentina.

Abstract in English not available.

NEWER CONCEPTS CONCERNING THE SYNDROME OF SHORT P-R INTERVAL AND WIDE QRS COMPLEX.—Juan Govea Peña, M.D., Havana, Cuba.

Abstract in English not available.

CARDIAC LESIONS IN RHEUMATOID ARTHRITIS.—Irving Graef, M.D., Daniel V. Hickey, M.D., and Vladimir Altmann, M.D., New York, N. Y.

The protocols and available microscopic sections of the heart were reviewed for cardiac lesions in sixty-six cases of rheumatoid arthritis studied at necropsy between 1939 and 1948 at the Goldwater Memorial Hospital, Welfare Island, New York City.

There were thirty men and thirty-six women distributed according to age between the third and ninth decades. The mean age for both groups was in the seventh decade; the mode of their distribution fell in the sixth and seventh decades. Antecedent rheumatic fever was reported in the history of one patient.

Gross valvular deformities were observed in twenty-nine cases; of these, nineteen were regarded as of the rheumatic type, but mild. In only one was there mitral stenosis. In five additional cases microscopic examination disclosed old rheumatic valvulitis. In two there were granulomatous zones of interstitial collagenous necrosis undistinguished from those seen in rheumatoid subcutaneous nodules.

Pericarditis consisting usually of old adhesive or obliterative lesions was found in one-half of the cases. In four, clinically unsuspected acute fibrinous pericarditis was found. In one a group of necrotic collagenous nodules with a granulomatous reaction like those seen in subcutaneous nodes was seen in histologic preparations.

Myocardial lesions included seven instances with active chronic inflammatory interstitial myocarditis. Among these there were five of the granulomatous type which resembled Aschoff nodules. In addition, perivascular fibrosis of significant degree and characteristically arranged in "onionskin" layers was found in about two-fifths of the cases. In two cases lesions like those of periarteritis nodosa were found in the coronary arteries, although periarteritis nodosa was unsuspected ante mortem.

On the basis of these results there were twenty-six cases with definite rheumatic types of cardiac lesions and nine others which were probably rheumatic, but in them the evidence was not conclusive. These data indicate that careful study of the heart in rheumatoid arthritis is warranted, even in the absence of overt clinical or gross pathologic deformities. The evidence of cardiac involvement resembles that seen in rheumatic fever, but is less diffuse or severe, as a rule.

A COMPARISON OF PRECORDIAL ELECTROCARDIOGRAMS OBTAINED WITH CR, CL, CF, AND V LEADS.—Sidney Grau, M.D., Martin Dolgin, M.D., and Louis N. Katz, M.D., Chicago, Ill.

Published in full, Am. Heart J. 37: 343, 1949.

THE VALUE OF DIET IN THE MANAGEMENT OF HYPERTENSION.—IRVING GREENFIELD, M.D., WOODMERE, N. Y.

Twenty patients in the fifth and sixth decades, with long-standing hypertension, have been observed. Therapy consisted of a low-sodium diet modeled after the Kempner regime. Control studies included history, physical examination, teleroentgenograms, electrocardiograms, blood count, blood chemistry, and urinalysis. These patients were observed as ambulatory patients and studies were limited to those procedures which could be carried out in the management of the ambulatory patient seen in the office of the physician. The beneficial effects seen in the teleroentgenogram, electrocardiogram, and blood pressure will be presented. The reversibility of hypertensive cardiac disease will be demonstrated. In a small group of these patients, the beneficial effects of this regime were obtained, but during the course of management, dietary indiscretions were committed; data will be presented to show the unfavorable effects of these dietary indiscretions as well as the reversibility of these changes with resumption of diet. In the decompensated patient with hypertensive cardiovascular disease, the beneficial effects of this regime on water retention with resulting diminution in the required maintenance dose of digitalis will be noted.

THE ETIOLOGY OF PERICARDITIS.—GEORGE C. GRIFFITH, M.D., AND LEON WALLACE, M.D., LOS ANGELES, CALIF.

Approximately fifty years ago Preble analyzed the etiological factors in 244 cases of pericarditis. With more effective methods of treatment, the etiological factors should be altered and the incidence of certain causative agents lowered.

Source of Material.—A survey of 13,353 consecutive autopsies performed in the Los Angeles County Hospital during the seven years 1940 through 1946 was carefully reviewed with reference to the etiology of pericarditis.

Analysis of Data.—Seven hundred twenty-nine cases of pericarditis were found. This is a total incidence of 5.4 per cent.

Comment.—The general incidence of pericarditis is slightly higher than that reported by Smith and Willius in 1932. They reported an incidence of 4.2 per cent in 8,912 necropsies. Of the acute inflammatory types of pericarditis, nonspecific idiopathic pericarditis shows the highest incidence. If rheumatic pericarditis is added to the idiopathic pericarditis, the percentage equals the percentage incidence of rheumatic pericarditis reported fifty years ago by Preble. Tuberculous and pneumonic pericarditis have definitely decreased in frequency. Uremic pericarditis and pericarditis from acute and chronic coronary artery disease have definitely increased in frequency. Metastatic malignant disease involving the pericardium remains about the same each year.

The following conclusions are drawn: (1) The general incidence of pericarditis is 5.4 per cent. (2) Tuberculous and pneumonic pericarditis have definitely lessened. (3) Pericarditis of idiopathic and rheumatic origin is high in frequency. (4) The incidence of pericarditis secondary to uremia, coronary artery disease, and malignant diseases is definitely increased.

TOMOGRAPHIC STUDY OF THE CONGENITAL DILATATION OF THE PULMONARY ARTERY.—ADAMO GRILLI, M.D., AND VITTORIO PUDDU, M.D., ROME, ITALY.

Tomographic studies on four female patients (from 36 to 50 years of age) gave a clear picture of the dilatation of the pulmonary artery and its branches and allowed localization of the lesion. Two patients showed a bilateral dilatation: one of these had an enlarged heart with a contour similar to that of the classical picture of interauricular septal defect. The other two patients had a unilateral or predominant dilatation of the left branch; the heart was little enlarged in both cases.

THE ANALYSIS OF THE CARDIOGRAM OBTAINED WITH IMPROVED TECHNIQUE.—FRANZ M. GROEDEL, M.D., NEW YORK, N. Y.

The cardiogram, the record of the cardiac concussion of the chest wall, in older times highly valued, is hardly mentioned in modern literature. Technical difficulties discouraged physicians from continuing the use of this clinical method. The technique of electrical pulse recording with special microphones, conceived by the author, facilitated cardiography greatly. The special receiver bell, developed for phlebography, was fastened to the chest and varied determinable pressure was exerted on the bell. Analysis of cardiogram and phlebogram, with the aid of simultaneously recorded cardiophonograms and electrocardiograms, was routinely exercised for several years.

Results.—The conception that the cardiogram records only the ventricular movements must be discarded. The cardiogram, when recorded with this sensitive method—just like the phlebogram—mirrors every mechanical cardiac event occurring during one heart cycle and, frequently, is even more differentiated than the phlebogram. The isometric and isotonic contraction of each ventricle, the various systolic phases, the opening and closing of each valve, the movements of each auricle, the mechanical event causing the third sound, are reflected in most cardiograms. Characteristic differences in configuration exist over the various chest areas and between the normal and diseased heart.

THE USE OF A SPOT FILM RADIOGRAPHIC DEVICE IN CARDIAC ROENTGENOLOGY.—NATHAN GROSSMAN, M.D., MILWAUKEE, WIS.

Radiological examination of the heart calls for identification of the several chambers and segments of these chambers in the various views, namely, the posteroanterior, the left anterior oblique, and the right anterior oblique. Correlation with the clinical picture gives the cardiologist an idea of the status of the myocardium from a dynamic standpoint. Examination of the various segments of these several chambers requires positioning of the patient with specific reference to each individual chamber in that the same oblique position is not satisfactory for the examination of chambers whose silhouette is present in a given view. Because of the requirements of line positioning, fluoroscopy has its greatest use. The disadvantage of this method is that no pemanent record for comparison or study is retained. It is suggested that the use of spot films of the various chambers and segments of these chambers be made in order to overcome the difficulty described. This would eliminate the personal equation to some extent and certainly would afford opportunities for subsequent comparison.

Technique and technical factors are described. Several illustrations are included. Advantages and disadvantages of the method are enumerated.

DYNAMICS OF THE INTERVENTRICULAR SEPTUM.—RICHARD GUBNER, M.D., HARRY E. UNGERLEIDER, M.D., AND IRVING HIRSHLEIFER, M.D., NEW YORK, N. Y.

The dynamic role of the interventricular septum has been largely overlooked because of its inaccessibility to study. The presence of large ventricular type pulsations along the right heart border in aortic insufficiency can be interpreted only as evidence of a powerful movement of the septum to the left in systole carrying the right side of the heart with it. More direct observation of the movement of the interventricular septum has been accomplished by roentgenkymographic study in the left anterior oblique position during contrast visualization of the heart chambers with Diodrast. With this technique whereby the septum is visualized, it is found that the excursion of the interventricular septum considerably exceeds that of the free left ventricular wall. It is evident that the

interventricular septum has a most important function in left ventricular contraction. The nature of the septal movement makes dubious the existence of the so-called Bernheim syndrome. The contrast roentgenkymographic technique yields much additional information, namely, the thickness of the left ventricular wall and the extent of systolic emptying of the ventricular cavity. It also permits study of cyclic blood flow changes in the auricles and great vessels.

EFFECTS OF IONS AND DRUGS UPON MYOCARDIAL RHYTHMS INDUCED AT THE ANODE AND CATHODE APPLIED TO THE MAMMALIAN VENTRICLE.—A. Sidney Harris, M.D., Houston, Texas.

Characteristics of the response of cardiac muscle at the anode and the cathode during the passage of direct currents have been reported. The modifications in those electrically induced reactions brought about by ions and drugs are being recorded to reveal (a) common properties as shown by ectopic thresholds and patterns and (b) factors that predispose to ventricular fibrillation or prevent it.

In dogs anesthetized with morphine and a minimal dose of barbital sodium (180 mg. per kilogram), the cathodal response is regular ectopic tachycardia. The anodal response is short accelerating paroxysms which often lead quickly into ventricular fibrillation. Regular tachycardia seldom produces fibrillation.

The local application of drops of 1:1000 epinephrine hydrochloride at the stigmatic slightly lowers the cathodal threshold, the rhythm remaining regular. The anodal threshold is increased, and the tendency to accelerating responses is maintained or enhanced. The probability of fibrillation upon effective anodal stimulation is greater.

Drops of 5 per cent calcium chloride raise cathodal and anodal thresholds, the cathodal changing more. The cathodal rhythm usually remains regular. The anodal rhythm is changed by calcium ions from the accelerating type to a regular one. The probability of fibrillation is greatly diminished.

In dogs anesthetized with pentobarbital sodium, near-threshold cathodal stimulation often produces a coupled or bigeminal rhythm, considered indicative of recovery through supernormality. Anodal stimulation produces a regular and not accelerating rhythm. The probability of fibrillation is low.

In all tests the tendency to an accelerating rhythm upon anodal stimulation was associated with high probability of fibrillation, and a change to regular rhythm reduced this probability.

EXPERIMENTAL HYPERVOLEMIC HEART FAILURE.—Tinsley R. Harrison, M.D., Dallas, Texas.

Cardiac overload has been produced in dogs by the intravenous administration of large volumes of albumin solution or of blood. The point at which the cardiac output fails to continue increasing or begins to decline, despite the continued further rise in venous pressure, has been taken as the point indicating the onset of heart failure. The comparison of these results with those found in the ordinary types of clinical heart failure would indicate one of two possible conclusions: (a) Either one must conclude that there are multiple types of heart failure with multiple fundamental hemodynamic disturbances, or (b) if a single hemodynamic defect exists in all types of heart failure, this is a defective response in relation to filling load. The latter assumption is in keeping with the classical physiological and clinical concepts. If this assumption is correct, such factors as inadequate tissue blood supply, diminished renal blood flow, and so forth, are to be regarded as secondary, although at times very important factors.

RHEUMATIC FEVER IN HAWAII.—ALFRED S. HARTWELL, M.D., HONOLULU, T. H., HAWAII.

A brief summary of the geographic location, temperature, and rainfall of Hawaii is given. The variegated population and racial percentages are shown. Until ten years ago rheumatic fever was thought not to exist in Hawaii. Recently interest has increased. A five-year study of hospital admissions for heart disease in Honolulu is described. A total of 1,269 cases were studied: 218 (17.1 per cent) had rheumatic heart disease or rheumatic fever. There were 330 admissions among these patients, or 0.4 per cent of 81,949 patients admitted to the medical services of four hospitals.

Fifty-one of the rheumatic patients died, a mortality of 23.4 per cent. Sex, age, and racial origin are discussed. One hundred sixty-three (74.7 per cent) were born and lived in Hawaii. Those with cardiac involvement (89.9 per cent), the valves involved, the incidence or pericarditis (9.1 per cent), auricular fibrillation (16.1 per cent), chorea (2.3 per cent), congestive failure (18.2 per cent), and active carditis (35.3 per cent) are shown.

Rheumatic fever in Hawaii is a mild disease, rarely showing acute arthritis or high fever.

ON CHANGES OF THE T WAVE AND THE RS-T SEGMENT OF THE HUMAN ELECTROCARDIOGRAM.—HANS H. HECHT, M.D., SALT LAKE CITY, UTAH.

The electrical behavior of isolated nerve and muscle cells, the results obtained from animal experiments, and induced alterations of the human endo- and epicardial electrocardiogram suggest that the majority, if not all, of the RS-T segment shifts and T-wave changes are governed by four basic factors: (1) Slowing the rate of repolarization (lengthening the duration of the activated state) of subepicardial regions results in inversion of the terminal portion of T in epicardial leads or in leads to which the electrical effects of epicardial regions are being deflected ("ischemia"). (2) Similar processes occurring endocardially manifest themselves in epicardial leads by increasing the height of T or by uprighting a previously inverted T wave ("paradoxical reversal"). (3) Lesions of greater intensity result in incomplete repolarization of the region injured and in flow of electrical currents at rest ("injury"). Subepicardial lesions are characterized by an apparent elevation of the RS-T segment in epicardial leads while (4) depression of RS-T in such leads signals intense alterations of the endocardial surface.

A number of procedures known to alter the rate of repolarization which were carried out in subjects with normal and abnormal resting electrocardiograms demonstrate that these concepts are applicable to the human heart. It may be shown that spontaneous RS-T segment shifts and T-wave changes may be viewed as combinations and mixtures of endocardial and epicardial "repolarization delay" (ischemia) and endocardial and epicardial "resting currents" (injury). A rational interpretation of T-wave changes in general appears feasible on this basis.

ELECTROCARDIOGRAPHIC CHANGES FOLLOWING ELECTROSHOCK THERAPY IN CURARIZED PATIENTS.—MILTON R. HEJTMANCIK, M.D., ALEXANDER J. BANKHEAD, M.D., AND GEORGE H. HERRMANN, M.D., GALVESTON, TEXAS.

To be published in full in *American Heart Journal.*

STUDIES ON THE PROPAGATION OF THE PULSE INTO THE MINUTE SKIN ARTERIES.—ALRICK B. HERTZMAN, M.D., ST. LOUIS, MO.

Under normal conditions, the contour of the skin pulse as recorded photoelectrically resembles closely that of the pulse in the parent arteries. (Compare the finger pad pulses with those in the digital and radial arteries.) Changes in the contour of the skin pulse depend less on the resistance in the minute arteries than on the ratio of the resistances in these and the parent arteries. Thus, dicrotism in the skin pulses results from the dilatations due to heat and Mecholyl but not from that induced by histamine, although the increase in blood flow from the two drugs is approximately equal. Again, during the early phase of the reactive dilatation from cold the pulses of the finger pad are extremly rounded until the digital artery begins to dilate. Similar but less marked rounding of the skin pulse occurs in hypertension and in peripheral arterial diseases. These changes in contour can be induced in normal subjects by compression of the digital artery with Gartner's capsules of varying length and inflated to various pressures. The use of these changes in contour in the location of sites of resistance to flow will be discussed.

ON HEART SYNAPTIC BLOCKING SUBSTANCES.—C. HEYMANS, M.D., GHENT, BELGIUM.

Several substances, including nicotine, acetylcholine, eserine, and Prostigmine, may block the conduction of the heart synapses, generally after a primary period of synaptic stimulation. Several drugs have been tested in order to investigate their action on synaptic transmission and excitability in the heart. These experimental investigations performed in dogs showed:

1. Di-isopropyl fluorophosphate (DFP) first stimulates the vagus synapses and may block further the vagal synaptic transmission and excitability. These effects are not related to the anticholinesterase influences of DFP.
2. Diethylamino-ethyl ester of phenyl-cyclopentane carbonic acid blocks the vagal and sympathetic synaptic transmission and excitability, without affecting the postsynaptic elements. Vagal stimulation, nicotine and DFP then have no effect on the heart rate, but acetylcholine still induces bradycardia. Higher doses also paralyze the postsynaptic vagal innervation and suppress the acetylcholine bradycardia.
3. Tubocurarine and the synthetic curarizing substances, di-iodo-ethyl of bis (quinoline-oxy-8')-1-5 pentane and tri-iodo-tri (triethyl-ammonium-methoxy) 1-2-3 benzene, in given doses, paralyze the cardiac vagal synapses.
4. Tetra-ethyl ammonium paralyzes the cardiac vagal, but not the cardiac sympathetic synapses. After this, neither vagal stimulation, nor nicotine, nor DFP will slow the heart, but acetylcholine still induces bradycardia.
5. Dibenzyl-dichlorothylamine (Dibenamine) does not paralyze the vagal synapses of the heart.

THE SYRACUSE AREA RHEUMATIC FEVER PROGRAM.—J. G. FRED HISS, M.D., SYRACUSE, N. Y.

A description of rheumatic fever program as developed in the Syracuse area will be presented. The sponsoring organization (The Rheumatic Fever Foundation) was chartered by the State of New York, Oct. 26, 1945, and is supported by membership dues and voluntary contributions. The program is organized in six basic parts, as follows: (1) program of professional and lay education, (2) diagnostic clinic, (3) special rheumatic fever hospital, (4) follow-up clinic, (5) case-finding program, and (6) research.

THE EFFECT OF A LOW FAT DIET ON THE SPONTANEOUSLY OCCURRING ARTERIOSCLEROSIS OF THE CHICKEN.—Louis Horlick, M.D., and Louis N. Katz, M.D., Chicago, Ill.

To be published in full in *American Heart Journal.*

SPLANCHNICECTOMY IN RELATION TO HYPERTENSIVE DISEASE OF PREGNANCY.—Emil M. Isberg, M.D., and Max M. Peet, M.D., Ann Arbor, Mich.

The large number of hypertensive women who were treated by splanchnicectomy at the University of Michigan Hospital presented the opportunity to investigate several aspects of the incompletely understood entity of hypertensive disease of pregnancy, especially in its relation to the autonomic nervous system and the operation of bilateral supradiaphragmatic splanchnicectomy.

The findings of this study strongly suggest that the surgical procedure of splanchnicectomy is worthy of being utilized in the management of some of the problems of hypertensive disease of pregnancy for the following reasons:

1. Not a single one of eighteen hypertensive women who responded to splanchnicectomy by maintaining normal blood pressure levels after operation and who subsequently became pregnant developed a toxemia of pregnancy.
2. Two cases of toxemia superimposed upon prepregnant hypertension and operated upon during pregnancy responded dramatically to splanchnicectomy, with prompt disappearance of the toxemias and the achievement of normal blood pressure levels for the remainder of the pregnancies and during a long postpartum follow-up period.
3. Women whose hypertension was first recognized during pregnancy manifested a better response to splanchnicectomy than did women whose hypertensive disease bore no relation to pregnancy, even though the clinical pictures of the two groups are alike prior to operation.

HEART DISEASE OF PREGNANCY.—Julius Jensen, M.D., St. Louis, Mo.

The paper considers the pathological effects of pregnancy on the cardiovascular system. Evidence has been accumulated in the literature recently that pregnancy, as such, may have effects on the myocardium which lead to the development of definite pathological changes in the heart muscle and, clinically, to congestive heart failure, which may occur during pregnancy, with or without association with hypertension, and also post partum. It is possible that this process is related to changes in the blood pressure and in the electrocardiogram which are sometimes seen associated with childbearing.

Several personal experiences, including electrocardiographic observations, form the original contribution to this subject.

ACTIVE PARTICIPATION OF THE ARTERIAL WALL IN ARTERIAL PRESSURE ADJUSTMENT.—C. Jiménez-Díaz, M.D., P. Barreda, M.D., and A. F. Molina, M.D., Madrid, Spain.

Stimulation of the central end of the vagi is used as a test to produce sharp arterial hypertension in the anesthetized dog. This effect is not suppressed even when the pituitary gland, the kidneys, and the adrenals are removed. Conversely, it disappears when the cervical spinal cord is sectioned. It is, therefore, the result of a reflex whose afferent path is the sensitive vagus, and whose efferent path is the sympathetic nerves. The humoral nature of the sympathetic action on the arterial wall is shown in crossed-circulation experiments, with simultaneous hypertension in the receptor dog when the vagi are stimulated in the

donor; and also by the fact that in the plasma of the dog there are present during the hypertension substances with vasoconstrictor action on the Lewen-Trendelenburg preparation of the frog.

In the experimental animal in which the upper and lower halves of the body have been separated, except for the nervous system, the former fed by the heart and the latter by pump perfusion, hypertension was produced also in the lower half by stimulation of the vagus, simultaneously with the increase of blood pressure in the upper half. But this only takes place if the lower half is perfused with dog plasma; if it is perfused with normal saline, the blood pressure does not increase.

It may be concluded from these experiences that the nervous action on the arterial wall frees something which acts on the plasma to produce the hypertensive substance. Through analogy with the system from the ischemic kidney it is admitted that the material from the artery is a ferment, "arterin," that acts upon the hypertensinogen of the plasma to produce the "arteriohypertensin," a fundamental factor in the regulation of pressure and tone of arteries. Arterial extracts that have no hypertensive action acquire it when incubated together with plasma "hypertonogen" of the same animal. This effect is very similar to the renal hypertensin and is also potentiated by cocaine. The meaning of this humoral-enzymatic mechanism regulating blood pressure is discussed.

SUBACUTE ABACTERIAL ENDOCARDITIS.—C. Jiménez-Díaz, M.D., E. Arjona, M.D., and E. Lopez-Garcia, M.D., Madrid, Spain.

The authors have described their observations on patients with a clinical picture quite similar to that of bacterial endocarditis, with a febrile course and a malignant evolution, in which blood cultures are persistently negative. This is called "subacute abacterial endocarditis."

The clinical picture has been based upon forty-one detailed cases, analyzing the differences and similarities to bacterial endocarditis. A presumptive differential diagnosis is clinically possible, strengthened by negative blood cultures. The pathological study stresses the distinctive character of this kind of endocarditis, first described by these authors. Cultures of the cardiac valves and of other organs have also always been negative. Certain differential characteristics are also found in the histological study.

The relationship between Libman's bacteria-free stage and the indeterminate endocarditis of Gross and Friedberg is discussed, and it is concluded that an active infection by an organism that cannot be isolated with current techniques is being dealt with (malignant rheumatic fever, associated virus, or rickettsia?).

Attention is drawn to penicillin resistance which requires very high doses to obtain beneficial results.

CARDIOVASCULAR EPILEPSY.—Fuad Kandalla, M.D., Bagdad, Iraq.

Atypical cardiovascular emergencies intractable to known cardiac drugs may be due to atypical epilepsy. The diencephalon controls the cardiovascular system as well as the central nervous system. Diencephalic epilepsy may simulate cardiovascular arrhythmias. In such a case, intravenous injection of sodium phenobarbital might be a life-saving measure, replacing digitalis, ouabain, mercurial diuretics, quinidine, or even adrenalin. This does not mean that one should give first choice to anticonvulsant drugs, but rather that they should be considered in case of unexpected failure of cardiotonic drugs.

Cardiovascular epilepsy may be genetic (complete or incomplete) or agenetic (complete or incomplete). Clinical types consist of (1) vasomotor anginal epilepsy, (2) paroxysmal tachycardial epilepsy, and (3) hypertensive encephalo-

pathic epilepsy. A migrainoid type is also described. Agenetic epilepsy (latent) is precipitated by nervous tension or coronary vasomotor constriction.

The chief symptom is cardiac pain without effort and without demonstrable organic cardiac disease. There is a definite familial history of epilepsy. The treatment is the use of barbiturates. If diabetes, nephritis, arteriosclerosis, cardiac enlargement, or other diseases are present, these should be treated.

CHRONIC COR PULMONALE DUE TO BILHARZIAL PULMONARY OBLITERATIVE ARTERIOLITIS.—M. R. KENAWY, M.D., CAIRO, EGYPT.

To be published in full in the *American Heart Journal*.

THE CORONARY VASODILATOR ACTION OF KHELLIN.—G. V. ANREP, M.D., M. R., KENAWY, M.D., AND G. S. BARSOUM, M.D., CAIRO, EGYPT.

Published in full in this issue.

TRANSMISSION OF SOUNDS IN CARDIOVASCULAR DISEASE.—WILLIAM J. KERR, M.D., SAN FRANCISCO, CALIF.

Demonstration by lantern slides of murmurs in aortic stenosis and two of the commoner congenital lesions, patent ductus arteriosus and coarctation of the aorta, shows the value of time relationships to the ventricular systole in diagnosing these clinical conditions. The use of techniques at the bedside will be discussed whereby differentiation can be achieved. The symballophone, a modified and double stethoscope, permits comparison of sounds and determination of time relationships essential to the examination.

NEW APPLICATIONS OF CHEST LEAD DIAGRAMS AND CIRCUMFERENTIAL LEADS IN CLINICAL CARDIOLOGY.—BRUNO KISCH, M.D., NEW YORK, N. Y.

The author has previously described the use of chest lead diagrams for the graphic registration of electrocardiographic changes in circumferential leads. In 200 not yet published complete chest explorations in human beings, done in collaboration with Dr. B. Richman, and in not yet published animal experiments, the following findings were obtained.

The chest lead diagram shows, as a rule, a typical configuration in cases with left axis deviation due to hypertrophy of the left ventricle which is different from that due to positional change of the heart. New data confirm the previous statement that in posterior wall infarction a QS pattern is found, as a rule, on the right side of the chest chiefly or exclusively in CL leads. In patients with hypertensive patterns in the standard leads (high voltage and widening of QRS, depressed RS-T segment in Lead I, and inverted T_1), a QS pattern is also found on the right side of the chest but chiefly or exclusively in CF leads.

The studies of recent material again support the opinion that in cases of right axis deviation and in right ventricular hypertrophy the high R or R′ on the right side (mainly present in CL), which decreases the nearer the electrode approaches the sternum, is produced by the left ventricle. The first R in cases with R′ is the R of the right ventricle.

The statement made many years ago and since confirmed by other authors that whenever depression of the RS-T segment appears anywhere in the chest leads in man or in animal experiments, or in direct leads, an opposite place on the heart or chest can be found with elevation of the RS-T segment is proved again. This can be applied to cases of coronary thrombosis as well as coronary insufficiency and proves helpful in the localization of the damaged area.

ON THE MEASUREMENT OF THE QRS COMPLEX AND THE INTERPRETATION THEREOF BY DIRECT AND INDIRECT DEDUCTION.—J. B. KLEYN, M.D., AND R. M. F. HOUTAPPEL, THE HAGUE, HOLLAND.

To be published in full in *American Heart Journal*.

VARIABILITY OF ENDOCARDIAL POTENTIALS OF THE RIGHT VENTRICLE.—CHARLES E. KOSSMANN, M.D., ADOLPH R. BERGER, M.D., J. BRUMLIK, M.D., STANLEY BRILLER, M.D., and BERTHA RADER, M.D., NEW YORK, N. Y.

In the course of a series of experiments concerned with the determination of the action potentials developed in the interior of the heart in man, it was noted that the nature of the deflections obtained, particularly in abnormal hearts, depended upon the location of the electrode in the cavity of the right ventricle. This was particularly true when standard and precordial leads suggested block of the right bundle branch. In order to support the accuracy of this belief, the following procedure was instituted in several patients:

The electrode was introduced into the pulmonary artery. Then with the potential being recorded from the interior simultaneously with a fixed lead from the exterior (usually standard Lead I), a continuous record was made as the electrode was slowly withdrawn from the pulmonary artery into the right ventricle, then into the right atrium, and finally into the superior vena cava. By this technique an exploration was made of the right side of the interventricular septum, usually from the upper end of the outflow tract, down to the apex, and then along the inflow tract into the tricuspid orifice.

The records obtained indicate considerable variation in the potential of the cavity of the right ventricle in patients with heart disease and emphasize the importance of drawing no conclusions from a lead made from a single location within this chamber. Records from the pulmonary artery and from the right atrium showed much less variation than those obtained from the right ventricular cavity.

RENAL DYNAMICS IN "ESSENTIAL" HYPERTENSION, THE EFFECT OF SYMPATHECTOMY.—MILTON LANDOWNE, M.D., ALF S. ALVING, M.D., and WRIGHT ADAMS, M.D., CHICAGO, ILL.

Simultaneous studies of blood pressure and Diodrast and inulin clearance were performed upon twelve patients with "essential" hypertension before and up to forty months after sympathectomy. In nine, nonsimultaneous measurements of cardiac output were made. Calculations were made of:

Rk = renal resistance ("afferent plus efferent arteriolar"),
R = resistance of the total measured circulation; and from these
Rn = nonrenal resistance.

If all the data are averaged, there is a slight reduction in renal blood flow after operation, with no essential change in resistances. However, if the cases are divided into three groups according to the changes in blood pressure after operation, differences between these groups become evident. The data may be interpreted as follows:

1. Both renal and total vascular resistances are increased in "essential" hypertension. Following sympathectomy, the renal resistance may be reduced, remain unchanged, or be increased.
2. The ratio of renal to nonrenal resistance is increased in some cases.
3. The lower the renal resistance, and the less disproportionate the renal to the nonrenal resistance, the greater the likelihood that sympathectomy may

result in a reduction in blood pressure. In such cases sympathectomy may not only effect a reduction in renal resistance, but a proportionately greater reduction in renal than in nonrenal resistance.

The assumptions intrinsic to the formulas used and the small number of subjects studied limit these interpretations to hypothesis.

AURICULAR FIBRILLATION WITH ANOMALOUS A-V CONDUCTION (WPW SYNDROME) IMITATING VENTRICULAR PAROXYSMAL TACHYCARDIA.—Richard Langendorf, M.D., Chicago, Ill.

Observations are reported on a case of mitral stenosis with the Wolff-Parkinson-White syndrome which presented auricular fibrillation and auricular flutter during a final phase of congestive failure. It is shown that the auricular impulses continue to be conducted to the ventricles either over the bundle of His or over the accessory bundle or over both pathways simultaneously giving rise to fusion beats. When conduction takes place exclusively over the accessory bundle, the ventricular rate tends to be very rapid and the record can be easily misinterpreted as ventricular paroxysmal tachycardia; when both types of ventricular complexes are present, those due to conduction via the accessory bundle tend to occur "prematurely" and in groups, imitating ventricular premature systoles. Records are presented showing such pseudobigeminy, trigeminy, and polygeminy. The reports in the literature of paroxysmal tachycardia of ventricular origin in cases of Wolff-Parkinson-White syndrome are reviewed and it is shown that the majority should be correctly interpreted as cases of paroxysmal auricular fibrillation with A-V conduction along the accessory bundle. It is pointed out that the rare occurrence of ventricular paroxysmal tachycardia in patients with this syndrome speaks against the hypothesis of an irritable focus in the ventricles; furthermore, the occurrence of anomalous A-V conduction in the presence of auricular fibrillation rules out the mechanical effect of auricular systole as a factor in the production of the syndrome. Quinidine sulfate was found to act predominantly on the transmission of the impulse via the accessory bundle, whereas digitalis affected predominantly conduction via the A-V node and bundle of His. Either drug used alone failed to slow the ventricular rate appreciably. The combined use of quinidine and digitalis seems to be the medication of choice to slow the ventricular rate in cases of the Wolff-Parkinson-White syndrome and permanent auricular fibrillation.

THE ELECTROCARDIOGRAPHIC PATTERN OF LATERAL WALL INFARCTION.—Richard Langendorf, M.D., Albert J. Simon, M.D, and Louis N. Katz, M.D., Chicago, Ill.

A clinical and electrocardiographic study is presented of thirty cases of recent lateral wall infarction. The diagnosis is based on the characteristic clinical picture associated with recent myocardial infarction and an electrocardiographic pattern characterized by discordant changes in chest Leads CF_2 and CF_5. Typical QRS changes are missing in most instances in the three chest leads (CF_2, CF_4, and CF_5) taken routinely; the S-T segment shows a tendency to be depressed in CF_2 and elevated in CF_5. The limb leads usually show the changes expected with anterior wall infarction; however in the "S-T stage" the changes may be less definite than in the chest leads; in the "T stage" reciprocity in Leads I and III is often missing and T is inverted in all limb leads. Thus, the previously described "T_N pattern" of healing myocardial infarction seems to indicate involvement of the lateral wall of the left ventricle. After recovery the residual electrocardiographic changes tend to take on a nonspecific appearance and no longer permit a diagnosis of remote myocardial infarction. An autopsy was obtained in two cases and confirmed in both instances the diagnosis of recent lateral wall infarction.

EXPERIMENTAL CHAGAS' HEART DISEASE.—F. S. Laranja, M.D., J. Pellegrino, M.D., and E. Dias, M.D., Rio de Janeiro, Brazil.

Electrocardiographic, x-ray, and pathologic studies of the heart were carried out on dogs experimentally inoculated with blood from human beings with Chagas' disease or with intestinal contents of bugs infected with *S. cruzi*.

Infected dogs developed a type of heart disease quite similar in several aspects to that found in human beings with Chagas' disease, in its acute and chronic stages.

Similarities between heart disease developed in experimentally infected dogs and that found in human beings with Chagas' disease were particularly striking in the chronic stage of infection. After several months of inoculation, dogs presented enlargement of the heart, particularly of the right cavities, several types of disturbance of cardiac rhythm, and signs of congestive heart failure, with dyspnea, gallop rhythm, edema, and ascites. Death in heart failure or sudden death occurred. The electrocardiographic changes observed in experimentally infected dogs included right bundle branch block, incomplete and complete; ventricular extrasystoles, bigeminal or trigeminal rhythm, or occurring in short runs (extrasystolic ventricular tachycardia); low grades of A-V block; transient A-V dissociation (isorhythmic dissociation); transient primary T-wave changes; atypical QRS changes; and patterns of right ventricular enlargement.

The possibility of reproducing in dogs a type of heart disease quite similar to that found in human beings with Chagas' disease, apart from furnishing convincing evidence as to the validity of the clinical description of chronic Chagas' heart disease as made by Chagas and recently by us, may open a fruitful field for collateral studies on heart disease.

OBSERVATIONS ON THE MECHANISM OF THE WOLFF-PARKINSON-WHITE SYNDROME (WPW) AND OTHER TYPES OF PRE-EXCITATION.—Eugene Lepeschkin, M.D., Burlington, Vt.

In thirty patients with the Wolff-Parkinson-White syndrome the potential of the entire chest surface was mapped by means of synchronized unipolar leads. The right or upper posterior hemithorax first develops steady negativity of low voltage. Negativity of high voltage then rotates across the precordium to the left. This indicates that the aberrant initial ventricular excitation originates near the A-V groove.

In one case (observed together with Dr. R. Fremont) P-R first became prolonged during rheumatic fever. A slow initial portion of QRS then appeared, making P-R normal and QRS prolonged. During convalescence P-R became shortened as in the typical Wolff-Parkinson-White syndrome. Here the slow initial portion of QRS was fixed to the rest of QRS, not to P, indicating that aberrant ventricular excitation took place after passage of the A-V node.

In many cases the appearance of the Wolff-Parkinson-White form was preceded or followed by terminal inversion of T in leads which had shown a downward slow initial portion of QRS. A similar relation exists between the direction of QRS and that of the subsequently appearing inverted T in paroxysmal ventricular tachycardia. This indicates local prolongation of activity in regions where the aberrant excitation originates, making increased myocardial excitability due to myocarditis in these regions a possibility.

EXPERIMENTAL STUDY ON THE MECHANISM OF THE CARDIAC MONOPHASIC ACTION POTENTIAL (MAP).—Eugene Lepeschkin, M.D., Burlington, Vt.

1. In frogs and cats the slow "extrinsic" component of the electrocardiogram registered by means of suction electrodes remained unchanged after appli-

cation of suction, but the rapid "intrinsic" component was reversed in direction. The monophasic action potential began when the excitation reached the "normal" electrode, but the difference between the curves between and after injury was reached. The duration of ascent of this monophasic deformation curve decreases with the diameter of the suction electrode and reaches 0.006 second if microelectrodes are used. This apparently corresponds to the ascent of activity in the single muscle fiber.

2. If the muscle surface reverses its polarization during excitation, the muscle interior becoming positive (Curtis and Cole), rapid injury during systole should cause instantaneously a positive injury potential. Actually a positive potential did not develop until the end of systole, when it could be attributed to accelerated repolarization. The fact that the positive monophasic action potential is usually greater than the negative diastolic injury potential must be attributed, in accordance with Katz, to partial depolarization in the vicinity of the injury.

3. If a U wave was present before injury, it was transformed into a negative afterpotential after injury.

CIRCULATORY MODIFICATIONS IN MAN AFTER INGESTION OR INFUSION OF FLUID.—JEAN LEQUIME, M.D., BRUSSELS, BELGIUM.

1. After the ingestion of 1.0 liter of water, a considerable increase of the cardiac output, and a still larger increase of the systolic output are observed. Thus, the intake of a great amount of fluid results in an increase in cardiac work, and this must be considered in patients with a deficient myocardium. The observed variations are not necessarily related to diuresis, since saline gives a slight diuresis, while water gives a rapid and intense diuresis. They are not the result of an increase of metabolism, for the oxygen consumption does not change noticeably. The increase of the cardiac output should be the result of the increase of the blood volume and of cutaneous, splanchnic, and renal vasodilatation.

2. After intravenous injection of forty c.c. of a 20 per cent sodium chloride solution in normal man, a cardiac acceleration is observed. Venous pressure is increased, the circulation rate is noticeably shorter, and there is a slight increase of the oxygen consumption. The arterial pressure does not undergo any significant changes. The cardiac output increases considerably, apparently because of vasodilatation, especially in the cutaneous tissues. In patients with coronary disease, injection of a saline solution frequently results in changes in the RS-T segment in the electrocardiogram similar to those observed after an exercise test or an anoxemia test. These electrocardiographic changes are probably due to a relative coronary insufficiency attendant upon a greatly increased cardiac output. This method is thus of value in the diagnosis of coronary disease.

ARCHITECTURE OF THE HUMAN VENTRICULAR MYOCARDIUM.—MAURICE LEV, M.D., CHICAGO, ILL., and S. SIMKINS, M.D., OMAHA, NEB.

By a combination of gross and microscopic studies of the human heart, during which the ventricular fibers were unrolled by a modification of Mall's technique, it was found that the concept that four distinct muscles (superficial and deep, sinospiral and bulbospiral) constitute the ventricular wall is in need of correction. The ventricular myocardium consists of one muscular syncytium, made up of fibers arranged in fasciculi of various sizes, both gross and microscopic, some of the former being grouped together to form bands. We have recognized three depths of fasciculi, epicardial, middle, and endocardial, without connotation that any connective tissue cleavage planes separate the syncytium into lamina. By the invagination of fasiculi, the septum is formed, thus demarcating right and left ventricular musculature. The musculature of both ventricles and the septum, however, are all part of one muscular syncytium.

SOME EFFECTS ON THE CIRCULATION OF SMOKING CIGARETTES WITH VARYING NICOTINE CONTENT.—Robert L. Levy, M.D., James A. L. Mathers, M.D., and Myron C. Patterson, M.D., New York, N. Y.

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INTRACARDIAC CATHETERIZATION IN THE STUDY OF CONGENITAL HEART DISEASE. I. FINDINGS IN INTERATRIAL SEPTAL DEFECTS.—Rudolfo Limó Lasón, M.D., and Víctor Rubio, M.D., With the Technical Assistance of Criseida Guerrero, M.D., Mexico, D.F., Mexico.

The catheter technique has been applied to the study of fifteen patients with auricular septal defects. Pulmonary, systemic, and shunt flows were calculated. The left auricle was catheterized in ten of our subjects; the pulmonary veins, in eight. The system of using the cavae-auricle oxygen difference will not give the diagnosis in all cases, as evidenced by the fact that the average oxygen difference in our series is 3.11 volumes per cent (range, 1.4 to 4.7).

Although the shunt has been considered to be from left to right, evidence is presented to the effect that in some patients, this may be altered in its entirety or in part. Some patients present, simultaneously, left to right and right to left shunts. This is proved by the fact that the blood taken from the right auricle is arterialized as compared with the average of both cavae, while the sample taken from the left auricle is mixed with venous blood as compared with samples taken from the pulmonary veins. One patient presented a complete reversal of flow; the shunt was directed entirely from right to left. In some patients the left to right shunt seems to increase in the erect position; the right auricle becomes more arterialized on standing.

STUDIES OF FLUOROCARDIOGRAPHY: TRACINGS OF THE LEFT VENTRICLE IN MYOCARDIAL INFARCTION.—Aldo A. Luisada, M.D., and Felix G. Fleischner, M.D., Boston, Mass.

Twenty patients with old or recent myocardial infarctions were studied by means of fluorocardiography. The graphic study was made in the postero-anterior position and in both anterior oblique positions.

Several abnormalities of ventricular systole and diastole were recognized. Among these, lack of pulsation and inverted pulsation (paradoxical pulsation) in a circumscribed area were considered as the most significant data; the former, pointing to an area of "local paralysis"; the latter, to a "dynamic aneurysm" of the ventricular wall. Evaluations of the dynamic results of such abnormalities are given. The reasons for suggesting the two new terms are discussed. Correlation of the findings with electrocardiographic data revealed a coincidence of about 90 per cent. In general, the area presenting an abnormality of contraction was found to be more extensive than indicated by the electrocardiogram.

The findings confirm those of previous roentgenkymographic studies. The reasons for a greater exactitude and broader applicability of fluorocardiography in comparison with roentgenkymography are given.

CONDUCTION IN RE-ENTRY PATHWAYS IN THE HUMAN HEART.—I. Mack, M.D., Chicago, Ill.

The phenomenon of re-entry was investigated by a study of the electrocardiogram of patients with ventricular premature systoles which showed so-called fixed coupling with the dominant beats. It was found that while in most patients a fairly fixed time interval was always present between the dominant

beat and the following ectopic ventricular systole, others showed variations in this time interval (labelled R-V interval). Parasystole as a possible underlying mechanism was excluded in the latter cases. The variations in the R-V interval were seen to be dependent on the cycle length immediately preceding it. In some instances the duration of the R-V interval varied with the length of the preceding cycle (prolongation of refractory period as a result of lengthening of preceding cycle), and in others it varied inversely with the length of the preceding cycle (effect of duration of rest period on conduction). In one of the latter cases partial block with 3:2 conduction and the Wenckebach phenomenon in the re-entry pathway was demonstrated. The subsequent development of 2:1 conduction, and eventually complete block (or interference) in the re-entry pathway was also seen.

BLOOD PRESSURE VARIATIONS IN PATIENTS WITH INTERMITTENT CLAUDICATION.—M. R. Malinow, M.D., B. Moia, M.D., E. Otero, M.D., and M. Rosenbaum, M.D., Buenos Aires, Argentina.

A hitherto undescribed mechanism of severe hypertension occurring in patients with intermittent claudication of the lower extremities is reported. A standardized leg exercise, sufficient to produce the characteristic pain, greatly raised the blood pressure of ten patients with intermittent claudication. Differences of 50 mm. Hg in the systolic and/or the diastolic were commonly found. Presumably, the same blood pressure variations occur while the patient is walking, thus greatly increasing the work of an already generally damaged heart. The same exercise did not greatly change the blood pressure in patients unless intermittent claudication developed. These blood pressure variations are reduced by vasodilator drugs (trinitrin, mannitol hexanitrate) and by tetra-ethyl ammonium chloride. The therapeutic implications are obvious. A method is described by which a standardized exercise of the legs is performed before and after a cuff at 280 mm. Hg is placed on the thigh. If the blood pressure variations so induced are compared, the presence or absence of ischemia can easily be detected.

PHENOMENA UNREVEALED BY ELECTROCARDIOGRAPHY WHICH ARE REVEALED BY X-RAY CINE-DENSIGRAPHY.—Maurice Marchal, M.D., Paris, France.

Abstract in English not available.

ELECTRO-HEMATOLOGY.—Frederico de Marco, M.D., Araraquara, E. S. Paulo, Brazil.

Abstract in English not available.

OBSERVATIONS ON BLOOD VOLUME AS DETERMINED BY PLASMA DYE DILUTION AND DILUTION OF RED CELLS TAGGED WITH RADIOACTIVE PHOSPHORUS.—H. S. Mayerson, M.D., Robert T. Niesset, M.D., and Champ Lyons, M.D., New Orleans, La.

Independent studies in patients on the rate of absorption and of loss of radioactive phosphorus by red cells in vivo and in vitro and of the loss of phosphorous from the plasma in vivo have been made to check the validity of red cell volume determinations by a simple dilution method, using radioactive phosphorous as a tracer. Whole blood samples are used for counting so that no chemical or physical separation of the trace element is required. Discrepancies between whole blood volume calculated from the red cell volumes and that calculated from the plasma volumes as determined by plasma dye (T-1824) are analyzed with refer-

ence to the ratio of plasma volume to red cell volume. Variations in plasma to cell volume ratios are shown to have opposite effects on the apparent volumes so that the results are not directly comparable. Total (body) hematocrits are obtained from the independent measurements of total plasma volume and total red cell volume and are compared with direct (in vitro) hematocrit readings made from peripheral blood. The variation appears to occur in either direction and to be nonspecific. The body and peripheral hematocrits often show reasonably good agreement in healthy individuals but usually show wide variation in disease. After transfusion there seems to be an unexpected loss in plasma volume and, in some experiments, evidence of trapping of red cells.

SYMPATHETIC COMPONENT OF THE ELECTROCARDIOGRAPHIC RESPONSE TO POSTURE.—H. S. MAYERSON, M.D., and HORACE L. WOLF, M.D., NEW ORLEANS, LA.

It was shown in a previous study that the tilting of an individual from the horizontal to the upright (75°) position produces an increase in the amplitude of P_2 and P_3, a decrease in T_1, T_2, and T_3 and T_{IVF}, a shift in the average QRS axis to the right and of the average T axis to the left, and a decrease in the QRS-T area. These results suggested that there are two phases of response to the alteration in posture. When the subject is tilted to the upright position, there is an immediate readjustment of the anatomic axis and a consequent reorientation of the electrical fields surrounding the heart which accounts for some of the changes. Subsequent variations which occurred during the maintenance of the upright position were interpreted as a manifestation of strong sympathetic activity evoked as a compensatory response to the diminished venous return and the tendency to cerebral anemia (and hypoxia).

The present experiments are a continuation of this study, particularly of the role of the sympathetic nerves in the response to tilting. Attempts were made to reinforce the sympathetic component by the administration of epinephrine and of atropine (to minimize or abolish parasympathetic influence). Conversely, ergotamine was administered to diminish or eliminate sympathetic activity and tetra-ethyl ammonium chloride (etamon chloride) was used to block all autonomic ganglia. Our results indicate that the electrocardiographic changes brought on by tilting to the upright position cannot be significantly modified by the use of these parasympatholytic, sympatholytic, or sympathetic reinforcing drugs. The assumption of the upright position evokes a strong sympathetic response which can be modified but not abolished by sympatholytic drugs. The latter diminish the vasomotor compensation but do not significantly alter the pulse rate increase which occurs with the change of position. The administration of a parasympatholytic drug (atropine) intensifies the sympathetic effect, as evidenced by an increased pulse rate over control studies.

THE APPLICATION OF MICROPLETHYSMOGRAPHY TO THE EVALUATION OF PATIENTS WITH HYPERTENSION.—R. S. MEGIBOW, M.D., AND A. S. W. TOUROFF, M.D., NEW YORK, N. Y.

Recently, we described an objective method which has proved of value in selecting hypertensive patients who would be benefited by thoracolumbar sympathectomy with splanchnicectomy. The procedure entailed an analysis of the volume changes in the toes and fingers before and after vasodilatation with nitroglycerine. Pulsatile and nonpulsatile volume fluctuations were recorded by means of a new ink writing photoelectric microplethysmograph.

The present investigation details modifications of the original technique. These consist of determining the rate of peripheral blood flow in addition to measuring the amplitude of both the volume pulse and alpha waves after nitro-

glycerine, and after two other vasodilators, namely, tetra-ethyl ammonium and dihydroergocornine. These drugs induce vasodilatation through different mechanisms, and on the basis of their pharmacologic effects, we have been able to separate patients with "essential" hypertension into two large categories. It has been found that those patients who develop maximal vasodilatation after tetra-ethyl ammonium rather than after nitroglycerine or dihydroergocornine prove to be the ones who will be most benefited by sympathectomy.

Illustrative plethysmograms will be demonstrated and certain concepts concerning the genesis and treatment of hypertension, formulated as a result of these studies, will be discussed.

FURTHER STUDIES ON THE ANTIFIBRILLATORY ACTION OF CORONARY DILATOR DRUGS IN CHLOROFORM-ADRENALINE VENTRICULAR FIBRILLATION.—K. I. Melville, M.D., Montreal, Canada.

In earlier publications from this laboratory, it was shown that the coronary dilator drugs, atabrine and papaverine, can protect the heart against ventricular fibrillation following injection of adrenaline during chloroform inhalation in dogs. It has also been shown that several coronary dilator agents can similarly prevent ventricular fibrillation induced by pituitary extract, a coronary constrictor agent, in phenobarbitalized animals. It was of interest, therefore, to study the influence of various other coronary dilator substances in chloroform-adrenaline ventricular fibrillation. The experiments to be described concern the influence of ephedrine, sodium nitrite, amyl nitrite, nitroglycerine, and diethylaminoethoxy-2-diphenyl (F-1262 or Dacorene) on this type of fibrillation.

Dogs anesthetized with sodium pentobarbital were used. Artificial respiration was maintained throughout by means of a Starling pump. In order to induce ventricular fibrillation, chloroform was administered for five minutes, following which adrenaline (0.02 mg. per kilogram) was injected. Smaller doses of adrenaline (0.002 mg. per kilogram) under similar conditions usually induced only ventricular extrasystoles but no fibrillation. The agent to be tested was injected during the chloroform inhalation, generally two to three minutes before the adrenaline. Blood pressure changes and electrocardiograms (Lead II) were recorded. In some animals the vagi were cut. All injections were made intravenously.

Under the described conditions, it was observed that ephedrine sulfate (2.5 to 5.0 mg. per kilogram), sodium nitrite (10 to 20 mg. per kilogram), amyl nitrite (15 to 20 secs. inhalation), nitroglycerine (0.1 to 0.5 mg. per kilogram), and diethylaminoethoxy-2-diphenyl hydrochloride protected the heart both from the cardiac irregularities observed after small doses of adrenaline and from fatal ventricular fibrillation after large doses of adrenaline. In a few experiments also, after induction of chloroform-adrenaline ventricular fibrillation, intracardiac injection of the latter compound in conjunction with cardiac massage stopped the fibrillation and a normal coordinated heart beat was restored. The blood pressure and electrocardiographic changes associated with these phenomena will be discussed.

The results appear to support the view that in chloroform-adrenaline ventricular fibrillation, impairment in myocardial nutrition is an important factor, and that the antifibrillatory actions of the agents used are due mainly to their coronary dilator actions. Whether this favorable effect of these drugs is due directly to offsetting some existing coronary constriction or indirectly to the improved blood supply to the myocardium cannot be stated.

CIRCULATORY EFFECTS OF A NEW SULPHURIC ESTER OF GLYCERIN.—Rafael Méndez, M.D., José Pisanty, M.D., and Ernesto Sodi P., M.D., Mexico, D.F., Mexico.

Trisulphoglycerin, synthesized from glycerin and Nordhausen's acid, causes the following effects:

1. In the anesthetized (Dial), eviscerated, and adrenalectomized cat, in maximal doses of 15 mg. per kilogram, there is a marked rise in arterial pressure (which lasts ten to thirty minutes), bradycardia, and often decreased pulmonary ventilation; probably due to bronchial spasm.
2. In the adrenalectomized dog, doses of 5.0 mg. per kilogram cause a clear hypertensive effect only after complete denervation of the carotid sinus and section of the vagi and depressor nerves. Higher doses produce cardiac irregularities which mask the pressor effect.
3. In the heart-lung preparation with heart failure induced by Nembutal, trisulphoglycerin in doses of 20 mg. produces a slight and transitory improvement, which appears as a decrease of venous pressure and a slight increase of output.
4. In the isolated rabbit ear a direct vasoconstrictor effect can be demonstrated.

Sulphuric esterification of glycerin and other radicals (new synthetic compounds under study) seems to confer hypertensive properties on the resulting compound.

NORMAL CIRCULATORY AND BLOOD VALUES IN ACCLIMATED PERSONS LIVING AT A HIGH ALTITUDE.—Jorge Meneses Hoyos, M.D., Mexico, D.F., Mexico.

Abstract in English not available.

THE ELECTROCARDIOGRAM IN EXPERIMENTAL ANOXIA.—Jorge Meneses Hoyos, M.D., Mexico, D.F., Mexico.

Abstract in English not available.

OBSERVATIONS ON THE SURVIVAL OF PATIENTS AFTER RECENT MYOCARDIAL INFARCTION—G. Y. Mills, M.D., F. Cisneros, M.D., Mexico, D.F., Mexico, and L. N. Katz, M.D., Chicago, Ill.

Five hundred seven patients with recent myocardial infarction were studied to determine the factors concerned in the long term prognosis. In five to six years 81 per cent of the patients were dead. About one-fourth of the patients died in the first two months, about one-half were dead at the end of a year, about two-thirds at the end of the third, and approximately four-fifths at the end of five years.

Hypertension on admission had no effect on the mortality rate in the first two months but caused a slight increase in the long term mortality. Similarly, the presence of known angina pectoris at the time of admission had no deleterious effect on the immediate mortality in the first two months, but the average duration of life of those dying after two months was somewhat shortened. In contrast, the presence of heart failure on admission sharply increased the immediate and over-all mortality rate and shortened the average duration of life of those dying after two months. The presence of diabetes mellitus on admission increased the immediate and over-all mortality rate but did not greatly alter the long term mortality. The absence of low voltage, heart block, ectopic rhythms, and sinus tachycardia caused a much better immediate prognosis, but the long term

prognosis was no better than for the whole group. Patients who were asymptomatic on admission had an immediate mortality rate little different from that for the entire group, but the long term mortality rate was better. The immediate mortality rate was greater for women, but after two months the mortality rate was less for women than men. The immediate mortality rate was little affected by location of infarct but after two months was better for lateral wall infarcts than for anterior and posterior infarcts.

THE ELECTROCARDIOGRAM IN "IN EXTREMIS." CLINICAL DEATH AND BIOLOGICAL DEATH.—Augusto Mispireta Dibarbout, M.D., Carlos Guibovich, M.D., and Jorge Neira, M.D., Lima, Peru.

Electrocardiograms were taken in human subjects (children and adults) and dogs in "in extremis," clinical death, and cellular or biological death. The death of the animals was produced by bleeding; human subjects died because of various diseases (two with skull fractures). Continuous electrocardiographic tracings were obtained, in some cases from the beginning of "in extremis."

We have differentiated, as other authors have done, the three periods: "in extremis," clinical death, and biological death. The last period was studied exclusively in relation to the cardiac electric activity. The time between clinical and biological death was variable with an average between three to seven minutes. The longest duration was fifty-four minutes, in a case of skull fracture. During "in extremis" there was always sinus tachycardia. Simultaneous with clinical death were the most varied modifications of rhythm, rate, and conduction. The final cardiac standstill occurred in one-half of the cases through auricular standstill and in the other one-half through ventricular standstill. Intracardiac injections of adrenalin did not significantly alter the electrocardiograms.

EFFECT OF THE INHALATION OF OXYGEN ON THE ELECTROCARDIOGRAPHIC CHANGES INDUCED BY EFFORT IN ANGINA PECTORIS.—B. Moia, M.D., and F. F. Batlle, M.D., Buenos Aires, Argentina.

Twelve patients with angina pectoris on effort and normal electrocardiograms at rest, but showing signs characteristic of myocardial ischemia on effort, were chosen for the study. Once the electrocardiogram became normal and after two hours rest following the effort, the same test was performed but having the patients inhale pure oxygen before, during, and after its execution. The electrocardiograms of the second test again showed changes similar to those previously registered. It is concluded, then, that the inhalation of 100 per cent oxygen is not capable of preventing the myocardial ischemia provoked by effort in anginal patients.

These findings confirm the general clinical impression which the authors have obtained from the use of oxygen administered correctly in concentrations varying from 50 to 100 per cent, during many years of practice, in patients with coronary diseases. They conclude that its therapeutic efficiency is slight or doubtful, except when there are disturbances of hemorespiratory function, a profound state of shock, or any other complication which would justify its use. This refers particularly to the use of the costly oxygen tent.

COMPARATIVE STUDIES ON THE ORAL AND INTRAVENOUS ADMINISTRATION OF DIGITALIS PURPUREA LEAF PREPARATIONS IN MAN.—B. Moia, M.D., and M. Monguel, M.D., Buenos Aires, Argentina.

The effects of oral and intravenous administration of digitalis leaf preparations were studied in numerous patients with permanent auricular fibrillation

and in normal subjects, by observing the modifications in cardiac rate and in the electrocardiogram.

Three types of comparative observations were carried out: (1) Digitalization with daily intravenous doses of 0.40 Gm. (exceptionally 0.60 Gm.) until a manifest therapeutic effect was obtained, attempting not to provoke vomiting, followed by a daily maintenance dose of 0.20 to 0.10 Gm. during ten days or more and then the same dose by mouth for fifteen or more days. (2) Similar doses to those in (2), but starting with the oral route and following with the intravenous. (3) In patients under chronic oral digitalization, administration of the same dose by the intravenous route for fifteen or more days.

The results obtained show that with these doses, the therapeutic and electrocardiographic effects, like those on heart rate in auricular fibrillation, are practically the same, whichever route is used.

THE USE OF FLUORESCEIN FOR THE ESTIMATION OF THE ADEQUACY OF BLOOD FLOW IN THE EXTREMITIES.—M. H. Nathanson, M.D., R. Merliss, M.D., and S. R. Elek, M.D., Los Angeles, Calif.

In a previous study it was shown that the circulation time to an extremity could be studied by the application of a histamine wheal on the extremity and the determination of the time of appearance of fluorescence in the wheal after the injection of fluorescein in an arm vein. There was a prolongation of this fluorescein-wheal circulation time in individuals with peripheral vascular disease. In the present report, the method has been extended to a larger number of patients and certain modifications have been followed and compared with the original procedure. In cases of peripheral gangrene in which amputation was considered, the fluorescein test was used to ascertain the line of demarcation between the skin receiving an adequate circulation and that to which the blood supply was definitely reduced. The use of multiple wheals demonstrated the point at which a definite prolongation of circulation time occurred. Another procedure was to make a linear scratch in the skin from above the knee to the ankle. Following the injection of fluorescein, a bright fluorescence is observed in the upper portion of the scratch, the fluorescence disappearing abruptly at a definite point. In the control extremity, good fluorescence can be seen throughout the entire length of the scratch. The results of amputation and the examination of the amputated extremities suggest that this provides a good method for the estimation of the adequacy of the circulation to the skin. An interpretation of circulation time measurements in terms of minute volume flow in the extremities is discussed.

STUDIES RELATIVE TO THE CHEMOTHERAPY OF BACTERIAL ENDOCARDITIS.—M. H. Nathanson, M.D., and R. A. Liebhold, M.D., Los Angeles, Calif.

The introduction of a successful therapeutic agent often leads to a clarification of the nature of a disease. The uniformly fatal character of bacterial endocarditis prior to the advent of penicillin and the failure of various therapeutic agents has not been adequately explained. It has been suggested that failure of antibacterial agents is due to an inhibiting or retarding effect by the fibrin on the diseased valves. In a previous study it was shown that sulfonamide compounds showed antibacterial activity on seeded agar plates but failed to do so on seeded fibrin plates. Penicillin was equally active on both media.

In the present study it was shown that fibrin or fibrinogen had no inhibiting action on sulfonamides, indicating that their inactivity was due to a failure to penetrate fibrin adequately. Also at autopsy fragments were taken from the

surface and deep portions of vegetations and placed on seeded agar plates. The zones of inhibitions surrounding the fragments were equal for the deep as compared with the surface portions, indicating a free diffusion of penicillin into the vegetation. In vitro studies demonstrated that streptomycin also diffuses freely into fibrin.

These studies indicate that the therapeutic efficiency of a compound in bacterial endocarditis depends on its ability to penetrate fibrin. The experiments also tend to minimize the importance of anticoagulants in this disease since fibrin has no retarding effect on the activity of penicillin and streptomycin.

THE CARDIOVASCULAR EFFECTS OF THE INTRANASAL ADMINISTRATION OF MECHOLYL.—M. H. Nathanson, M.D., and J. Tober, M.D., Los Angeles, Calif.

Supraventricular tachycardias are most effectively treated by stimulation of the vagus innervation to the heart. This may be accomplished (1) mechanically by pressure on the carotid sinus and (2) chemically by the administration of Mecholyl subcutaneously. These procedures require therapy by a physician or nurse. The effect of the sublingual administration of Mecholyl was studied. A local effect, salivation, was noted but no systemic effects were observed. However, on intranasal application of Mecholyl prompt systemic effects were observed. Such an action has previously been reported by Wright and his associates. The purpose of the present study was to determine whether the effects of a therapeutic dose of Mecholyl given subcutaneously could be produced by intranasal administration.

In a group of hypertensive patients Mecholyl was administered intranasally and subcutaneously. The depressor effect of 25 mg. subcutaneously could be completely and promptly produced by the administration of 200 to 300 mg. intranasally. The intensity of other systemic effects, flushing of face, sweating, salivation, and lacrimation, was the same after both methods of administration. On intranasal application, the action was as prompt as that observed after subcutaneous injection. Cardiac effects demonstrated by the electrocardiogram, such as varying degrees of heart block and cessation of auricular tachycardia, were observed after the intranasal administration of the drug. The conclusion is that a therapeutically effective dose of Mecholyl can be administered by the intranasal route.

THE PARADOXICAL EPINEPHRINE-ACETYLCHOLINE REACTION IN CORONARY INSUFFICIENCY.—Robert L. Nelson, M.D., Duluth, Minn.

Attention is directed to a physiologic mechanism which is an important factor in the production of some cases of acute coronary insufficiency. Certain persons display paradoxical responses to adrenalin and to acetylcholine. The usual response to adrenalin is an increased pulse rate, increased blood pressure, palpitation, and, in some cases, visible constriction of the retinal arteries or blanching of the skin. Acetyl-beta-methylcholine chloride usually produces the opposite effect.

In cholinergic individuals of high autonomic tone this is probably a more frequent mechanism in the production of coronary artery spasm than the literature indicates. It is probably one of the most easily prevented forms of coronary catastrophies and definitely one that should be recognized in all cases of autonomic study. A simple means of advance recognition and some clinical illustrations are presented.

THE BALLISTOCARDIOGRAPHIC PATTERN, WITH SPECIAL REFERENCE TO THE H-WAVE.—JOHN L. NICKERSON, M.D., NEW YORK, N. Y.

The origin of the various portions of the ballistocardiographic pattern is demonstrated by the use both of models and of clinical material. One serious objection to the model method of testing different circulatory situations has been that fluid ejection in the model produces immediate movements of the ballistic system, whereas with human ventricular ejection the movement of the ballistic system appears to be delayed by .02 to .03 second. In the work presented here we have been fortunate in obtaining records where the auricular and ventricular patterns were sufficiently separated so that the effect of the auricular complex in causing this apparent delay was revealed.

A CLASSIFICATION OF CONGENITAL CARDIAC DISEASES BASED UPON HEMODYNAMIC PRINCIPLES: ITS USEFULNESS FOR CLINICAL DIAGNOSIS.—SERGIO NOVELO, M.D., AND RODOLFÔ LIMÓN, M.D., MEXICO, D.F., MEXICO

It is considered that the alteration of circulatory dynamics in congenital cardiac cases is fundamentally responsible for the clinical and pathological findings. Regardless of the wide variety of anatomical types, the end result of the morphological defects is the creation of several circulatory patterns. Clinically speaking, it is not always possible to recognize the exact anatomical nature of circulatory alteration in most of the cases. Furthermore, surgery is able to correct or alleviate the altered circulation, either by surpressing anatomical defects or by creating compensatory mechanisms. Thus, in the present state of knowledge, what the clinician should accomplish is to individualize the patient's circulatory pattern and to ascertain if it is amenable to surgical correction. These facts stress the necessity of grouping congenital malformations of the heart within hemodynamic patterns. We believe that a classification of this sort will be useful in clinical work.

The authors present their own classification.

FURTHER STUDIES OF THE CIRCULATION WITH RADIOACTIVE ERYTHROCYTES.—GUSTAV NYLIN, M.D., AND S. HEDLUND, M.D., STOCKHOLM, SWEDEN.

Published in full in this issue.

MECHANISM IN WENCKEBACH'S PERIODS AND ELECTRICAL ALTERNANS.—RICHARD F. ÖHNELL, M.D., STOCKHOLM, SWEDEN.

Earlier studies regarding the mechanism in these conditions have emphasized the significance of insufficiency recovery from one beat to the other.

Öhnell and Anderson, 1946, and Öhnell, 1946, have reported cases where autonomic inhibitory effects seemed to dominate the picture in certain cases of Wenckebach periods. Periodicity was related to respiratory movements. The intimate connection with respiration has been further elucidated. Increased respiratory frequency gives fewer conducted beats per period. For a short while before the spontaneous disappearance of the periodicity, one period may occur at every other breath. "Aberrant" configuration of single periods may be explained by altered length of the respiratory cycles, and so forth.

As an explanation of this phenomenon, it is assumed that varying autonomic activity inhibits the A-V conduction. Furthermore, some mechanism or other will cause a return to a normal P-R interval after every dropped ventricular

beat. Electrical alternans may in some cases be due to the presence of an additional excitatory spread in the ventricles during every second beat ("concealed pre-excitation").

MECHANISM IN PRE-EXCITATION. THE "CACIVA" TECHNIQUE. ASSAY OF QUINIDINE EFFECT.—RICHARD F. ÖHNELL, M.D., STOCKHOLM, SWEDEN.

"Pre-excitation" indicates the presence of an abnormal (additional) excitatory spread in the ventricles, chronologically bound to auricular activity. It causes a slightly premature excitation of the area to which it spreads (Acta Med. Scandinav. suppl. 152, 1944).

By comparing the times required for depolarization of the ventricles during different functional states in the same case of pre-excitation, the role, if any, of the normally conducted wave from the auricles has been further elucidated. In sixteen or more of about eighty-five cases, the normally conducted wave seemed to play no role or only an inconspicuous one. In the majority of the pre-excitation cases, however, the abnormal as well as the normal wave participates in ventricular excitation during the pre-excitation beat. In but one of the sixteen cases was there a "kink" in the ascending limb of QRS. Comparatively late arrival rather than nonarrival of the normally conducted wave seems to explain its restricted role in these sixteen cases.

A report is given on the so-called Caciva technique, developed by the author. Different instruments (ten are presently available) are introduced into the thorax via a vein and an artery in the neck. Theoretical, diagnostic, and therapeutic problems are attacked in both dogs and man.

Öhnell and Obreschkov, 1948, used pre-excitation cases for biological assay of quinidine. However, there may be great variations in "quinidine need" from time to time in one and the same case. Öhnell, 1948, studied the part played by the auricles in pre-excitation. Kjellbeg and Öhnell, 1948, registered the movements of the x-ray heart shadow in pre-excitation cases as well as in cases with extrasystoles and impaired intraventricular conduction.

A STUDY OF ALLEGED INTER-CORONARY REFLEXES FOLLOWING CORONARY OCCLUSION.—DAVID F. OPDYKE, M.D., AND E. E. SELKURT, M.D., CLEVELAND, OHIO.

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BLOOD PRESSURES OF CHRONIC HYPERTENSIVE DOGS SURVIVING BILATERAL NEPHRECTOMY.—B. S. OPPENHEIMER, M.D., STEPHEN S. ROSENAK, M.D., AND GORDON D. OPPENHEIMER, M.D., NEW YORK, N. Y.

The failure of bilateral nephrectomy to abolish the experimental chronic hypertension of rabbits (Pickering) and of three dogs (Grollman) has previously been reported. The period of survival after bilateral nephrectomy was short; at most, four days in Pickering's experiments and three days in Grollman's.

By the use of peritoneal lavage (technique of Rosenak and Siwon, 1926) in three hypertensive dogs (Goldblatt method), the period of survival was prolonged by us to five, six, and nine days, respectively. In our three dogs which had been hypertensive for 1,055, 330, and 336 days previous to removal of the second kidney, the hypertension was maintained almost until death.

Peritoneal dialysis with a modification of Tyrode's solution was carried out on three dogs twice, twice, and three times, respectively, each time using about 20 liters over a period of seven hours. Substantial amounts of nitrogenous crystalloids were eliminated from the blood stream, in addition to which colloidal constitutents like proteins were washed out in considerable amounts. Thus,

in addition to the removal of crystalloid toxins and nitrogenous waste products, unknown high molecular substances were also removed from the blood stream. While the blood proteins were replenished from the body stores, after removal of both kidneys no such replacement of a humoral hypertensive factor originating from the kidney was possible. If a humoral hypertensive factor was still operative in maintaining hypertension, it should quickly disappear after bilateral nephrectomy because of the rapid destruction of the hypertensive substance.

INCIDENCE OF THE CARDIOPATHIES IN 1,138 CHILDREN OF THE PUBLIC SCHOOLS IN URUGUAYANA.—FRANCISCO ORCY, M.D., URUGUAYANA, BRAZIL.

1. Study of 1,138 children of the public schools in Uruguayana from April to August of 1947 revealed 146 suspected cardiacs, fourteen acquired organic cardiopathies, one congenital cardiopathy, and thirty-eight potential cardiacs, or, respectively, 12.82 per cent, 1.30 per cent, 0.008 per cent, and 3.33 per cent.

2. In the organic cardiopathies, rheumatic fever was the principal etiological factor; it appeared in ten of the fourteen cases (71.43 per cent).

3. In potential cardiacs, rheumatic fever was suspected in 50 per cent.

4. The congenital cardiopathy was a patent ductus arterious.

5. The sedimentation rate was increased in twelve acquired organic cardiopathies (85.71 per cent) and was normal in two. The Wassermann reaction was positive in one case, negative in twelve, and doubtful in four.

6. The sedimentation rate in potential cardiacs was increased in thirty-one cases (81.57 per cent) and was normal in seven. The Wassermann reaction was positive in one case, negative in thirty-three, and doubtful in four.

7. The incidence of organic cardiopathies was larger in subjects 9 to 12 years of age, with an average, respectively, of 17.12 and 15.75 per cent. Of the 1,138 children examined, male subjects (57.53 per cent) dominated over female subjects (42.45 per cent).

8. Among the cardiopathies there were seven cases of mitral cardiovalvulitis; aortitis was next frequent; and least frequent was cardiomyovalvulitis, three cases.

9. There were 101 phonoelectrocardiograms, of which eighty-six showed normal axis shift; eleven, deviation to the right; and four, to the left.

10. A history of epistaxis was found frequently in the patients with cardiopathies as well as in those with epidemic parotitis.

APEX BEAT IN RHEUMATIC AND LUETIC AORTIC INSUFFICIENCIES. ITS RELATION TO NECROPSY FINDINGS.—TEÓFILO ORTIZ Y RAMÍREZ, M.D., AND FRANCISCO GALLAND NAREDO, M.D., MÉXICO, D.F., MEXICO.

A comparative study has been made between the precordial data gathered from the palpation of the apex and the necropsy diagnosis in cases of aortic insufficiency of either rheumatic or syphilitic origin. In cases in which necropsy findings proved that the myocardial disturbances, most probably myocarditis existed, it was noticed that the apex beat possesses the classical characteristics of Bard's "dome apical impulse" only in pure rheumatic aortic insufficiency. This sign was investigated by radiologic and electrocardiographic study as well as by the clinical data in each case.

THE PARTICULAR IMPORTANCE OF SPECIAL ELECTROCARDIOGRAPHIC LEADS.—HAROLD E. B. PARDEE, M.D., NEW YORK, N. Y.

Precordial leads from the usual six precordial points are discussed, with emphasis on the general information about the heart's electrical activity to be obtained from precordial leads and the particular information to be gained from variations of the curve in different precordial areas. Special precordial points are recommended to record auricular activity. Esophageal leads are considered analogous to precordial leads; they merely lead off from a different aspect of the heart's surface.

The effect upon the precordial electrocardiogram of placing the remote electrode upon different limbs is studied in comparison with the use of the central terminal. A method is presented to determine from the deflections in the standard leads which extremity, when paired with any precordial point, will give the most negative (or least positive) deflection. Indications are deduced for the special value of CF leads, CR leads, CL leads, and V leads for different purposes.

Unipolar limb leads indicate the character and degree of modification of the precordial electrocardiogram to be expected when precordial points are paired with an electrode on the extremity. The information afforded by these leads regarding the electrocardiographic position of the heart is discussed and its relation to analogous information obtained from precordial leads. The contribution of unipolar limb leads to the diagnosis of myocardial disease is pointed out.

ON THE SIGNIFICANCE OF THE MIDDLE ARCH.—RAMIRO H. PAVÓN-CABALLERO, M.D., HOLGUIN, CUBA.

After reviewing the pathology of the left middle arch of the cardiac silhouette ("middle arch"), and after examining x-ray plates of our cases and those in the literature, we have reached the following conclusions:

1. The pathology of the "middle arch" is important and has its own characteristic picture.
2. It is the keystone in the diagnosis of congenital heart disease, both in children and adults.
3. It also has an important characteristic in mitral, congenital, or acquired disease.
4. X-ray plates showing any pathology of the middle arch must be followed in every case by oblique views and by frontal projections (both P-A and A-P), in order to establish its auricular, pulmonic, or aortic nature.
5. The angiocardiogram, especially the "levo-angiocardiogram" permits the determination of the extrinsic or intrinsic condition involved. Castellanos, Pereiras, and associates also detect hypertrophy of left lobe of the thymus by means of their procedure: the "pneumo-mediastino-anterior."
6. We adopt the classification of Castellanos and associates, as it is close to the true cardiological meaning.
7. We consider as cardiovascular those abnormal middle arches produced by myxedema and by thyrotoxicosis.

PERICARDITIS WITH ACTIVE PRIMARY GHON TUBERCULOSIS.—ALBERT A. F. PEEL, M.D., GLASGOW, SCOTLAND.

Two simultaneously observed cases are reported:

A previously healthy boy of 11 years developed a harsh cough, and examination revealed pericardial friction and effusion. X-ray films showed a primary active Ghon lesion in left upper lobe, hilar gland enlargement, and pericardial effusion. An electrocardiogram showed pericardial T-wave inversion and

"M complexes" in CR_2. Cough was his only symptom throughout; even when he was febrile, tachycardia was slight and he was bright and cheerful. The effusion absorbed in four weeks and so far (four months) there is no pericardial thickening.

A boy of 14, admitted with an active Ghon focus, hilar gland enlargement, and secondary infiltration of base of right upper lobe, had atypical rheumatism when 11 years of age and again two months before our observation. There was a mid-diastolic mitral murmur, slight convexity of pulmonary artery, and slight enlargement of left auricle. Pericardial friction developed after admission, lasted four days, and was not followed by effusion. The Mantoux test was positive. Leucocytes, 12,500; lymphocytes, 5,500 (44 per cent). He was afebrile with insignificant tachycardia. Four months later the heart shadow was normal but the secondary pulmonary lesion was extending.

The mildness of the constitutional symptoms, and the persistence of friction in the presence of effusion is stressed, reference being made to additional cases of acute tuberculous pericarditis. The etiology of Case 2 is discussed.

DISSECTING ANEURYSM OF THE INTERVENTRICULAR SEPTUM CAUSING OBSTRUCTION OF OUTFLOW TRACT OF RIGHT VENTRICLE, SECONDARY TO CORONARY OCCLUSION.—ALBERT A. F. PEEL, M.D., GLASGOW, SCOTLAND.

A woman, 59, who had had no previous cardiac symptoms, developed nausea, vomiting, and pain between the scapulae on April 5, 1946. Vomiting recurred four days later; no abnormality was noted in heart or lungs. She stayed in bed one week. On April 26, 1946, she suddenly became breathless and a loud cardiac murmur was noted. When she was referred ten days later, breathlessness was severe; she had a gray complexion, pale, cyanosed lips, congestion of the bases of the lungs, enlarged liver, and lumbar edema. The heart was enlarged with a widespread murmur suggesting the bruit de Roger, but no thrill. The pulse was barely perceptible, the blood pressure not measurable. She died the next day.

Autopsy showed old infarction at the apex of the left ventricle with more recent infarction of the interventricular septum. A round aperture at the upper anterior portion of the septum led into a disseting aneurysm; this tracked forward toward the right, then downward toward the apex, but without actually perforating into the right ventricle, from which it was separated by a thin layer of endo- and myocardium. It produced a sausage-shaped swelling projecting into the outflow tract of the right ventricle and caused mechanical obstruction.

CLINICAL SIGNIFICANCE OF THE DELAYED INSCRIPTION OF THE INTRINSIC DEFLECTION IN RIGHT PRECORDIAL LEADS.—RUBEN PELLÓN, M.D., AND DEMETRIO SODI-PALLARES, M.D., MEXICO, D.F., MEXICO.

The clinical significance of the delayed inscription of the intrinsic deflection (DID) is studied in the right precordial leads of 179 cases reaching autopsy. Intrinsic deflection above 0.04 second in V_1 was considered abnormal. The cases were classified into four groups:

Group I.—Valvular heart disease, 125 cases. In forty-seven cases with left valvular defects, the intrinsic deflection was found to be delayed in 12.7 per cent. In seventy-eight cases with added tricuspid lesions, the intrinsic deflection was delayed in 65 per cent. In heart diseases with valvular lesion, an intrinsic deflection delay in V_1 strongly suggests an added tricuspid lesion (fifty

out of fifty-six cases, or 89.2 per cent). Right bundle branch block was coincident with an added tricuspid lesion in six out of seven cases (85.7 per cent). Incomplete right bundle branch block had the same value in twelve out of thirteen cases (92 per cent).

Group II.—Cor pulmonale, fifteen cases. Delayed intrinsic deflection was found in 67 per cent. In five, intrinsic deflection was normal and two of these had left bundle branch block.

Group III.—Congenital heart disease, five cases. Three had a delayed intrinsic deflection, one each an Eisenmenger complex, cor biloculare, and transposition of the great vessels. Two had normal intrinsic deflection; the conditions were coarctation, patent foramen ovale.

Group IV.—Miscellaneous, thirty-four cases (glomerulonephritis, myocardial infarction, and so forth). There was no delayed initial deflection in 91.2 per cent and delayed initial deflection in 8.2 per cent (one of these had right bundle branch block). No correlation was found between delay in the initial deflection and the thickness of the right ventricular wall, nor with the degree of dilatation of the chamber.

PENICILLIN IN CARDIOVASCULAR SYPHILIS.—Aurelio Peralta V., M.D., and Luis Castaneda P., M.D., Lima, Peru.

Twenty-five patients were treated. Two had aortic insufficiencies (one in acute cardiac insufficiency), two had aneurysms, one had myocarditis, one had coronary stenosis (infarct) and aortitis, and some had coronaritis. Serial electrocardiograms and serological reactions were taken fifteen days after treatment and every two months. Penicillin "G" was used in increasing doses, 2,500 units being the initial dose, when there were evidences of coronary alterations. Higher doses, 50,000 to 100,000 units, were used. Total dose was 4,500,000 to 8,000,000 units.

Penicillin produced adverse clinical symptoms in 28 per cent; only in 3.9 per cent did they lead to pain. It was not necessary to stop treatment. In 7.8 per cent of those who presented clinical symptoms, electrocardiographic alterations appeared. However, these appeared without clinical symptoms. Moreover, they were temporary, disappearing eight to fifteen days later. One patient with cardiac insufficiency died one month after the end of the treatment.

The number of instances of increased and decreased serologic reactions were in equal proportion. The increase of the reactions had no relationship to the appearance of clinical or electrocardiographic abnormalities. When the serologic reactions diminished, they came back to their initial intensity four months later. Teleradiography did not change even after two years of treatment. Penicillin, although not harmless, can be used without danger to the patient's life.

REMARKS ABOUT 500 CASES OF CARDIOVASCULAR CONGENITAL MALFORMATIONS EXAMINED IN THE CARDIOLOGICAL DEPARTMENT OF THE INFANTS' MUNICIPAL HOSPITAL IN HAVANA DURING THE LAST THIRTEEN YEARS.—Rodolfo Perez de los Reyes, M.D., Horacio de la Torre, M.D., and Roberto Douglas, Havana, Cuba.

The authors present seventeen lantern slides in which they summarize the clinicostatistical data concerning 500 cases of congenital cardiovascular malformations.

THE SERIAL TOMOGRAPHIC STUDY OF THE THORAX IN THE DIAGNOSIS OF THE ANEURYSMS OF THE CONUS, TRUNK AND BRANCHES OF THE PULMONARY ARTERY.—ARMANDO PEREZ SIMON, M.D., AND FIDEL AGUIRRE, M.D., HAVANA, CUBA.

The usefulness of the tomography for the diagnosis of the dilatations of the conus, trunk, and branches of the pulmonary artery is demonstrated. Radiography and fluoroscopy give only superimposed pictures which cannot be studied apart. This is accomplished by tomography by means of a special technique which *localizes* the organ under study. When a bulging at the left border of the cardiovascular silhouette is noticed, it can be identified only with the tomographic cuts, which are made from the sternum to the vertebral column. Clinical cases of aneurysm of the conus and branches of the pulmonary artery are presented, with radiograms, kymograms, electrocardiograms, and serial tomograms, by means of which the diagnosis is made.

It is concluded that tomography offers a great contribution to the diagnosis of aneurysms and dilatations of the entire pulmonary artery tract. Its application is not difficult. In cases of aneurysm of the left branch of the pulmonary artery, only tomography makes it possible to observe whether there is a dilatation of the trunk. It is also very useful in cases of dilataion of the right branch. In one of our cases, the dilatation from the conus up to the divisions of the left branch was clearly visible, similar to an angiocardiogram.

PERIPHERAL ATERIAL EMBOLISM.—SAMUEL PERLOW, M.D., CHICAGO, ILL.

Forty cases of peripheral arterial embolism are reported; seven at the bifurcation of the aorta, twelve in the iliac, six in the femoral, six in the popliteal, one in the posttibial, five in the axillary, three in the branchial, and one in the ulnar artery. Of these, thirty-one (77.5 per cent) were due to auricular fibrillation, eight (20 per cent) to coronary thrombosis, and one (2.5 per cent) to subacute bacterial endocarditis.

Conservative treatment alone resulted in a viable extremity in twenty-five cases (62.5 per cent). Embolectomy after failure of conservative therapy resulted in improvement in two of seven cases, making a total of twenty-seven cases (67.5 per cent) improved.

Treatment consisted of: (1) Sympathetic block with procaine every two to four hours; (2) papaverine ½ to 1 grain intravenously every two hours; (3) anticoagulants, heparin, 50 to 100 mg. intravenously every four hours and Dicumarol, 300 mg. orally immediately; (4) whiskey as tolerated; (5) elevation of the head of bed to keep extremity dependent; (6) keeping room warm and wrapping the extremity in wool without external heat; (7) embolectomy after 4 to 8 hours' trial of conservative treatment.

AMPUTATION FOR PERIPHERAL VASCULAR DISEASE.—SAMUEL PERLOW, M.D., AND HAROLD A. ROTH, M.D., CHICAGO, ILL.

Analysis of 165 amputations for peripheral vascular disease performed at the Michael Reese Hospital during a twelve-year period (1936 through 1947) revealed an over-all mortality of 17.5 per cent. With the advent of penicillin and more frequent blood transfusions, the results improved and the mortality dropped from 25.0 per cent in 1936 to 1938 to 11.7 per cent in the period between 1945 and 1947. The element of sepsis has been eliminated for the most part and the recent deaths following amputation have been due mainly to cardiovascular accidents.

Local refrigeration of the gangrenous limb plus a proximal tourniquet has enabled us to tide the septic patients over the acute period and to carry out such preoperative measures as correction of the fluid and electrolyte balance, the ketosis and hyperglycemia, the hypoproteinemia, and the anemia, and to administer large doses of penicillin. By these means the amputation was changed from an emergency in a poor-risk patient to one of election in a properly prepared patient.

Preliminary lumbar sympathetic ganglionectomy permitted us to save the knee in a number of patients who would otherwise have required supracondylar amputation.

PATHOLOGY OF THE CARDIAC ATRIA. AN ANATOMIC-ELECTROCARDIOGRAPHIC CORRELATION BASED ON A STUDY OF EIGHTY-FIVE HUMAN HEARTS.—C. L. Pirani, M.D., and R. Langendorf, M.D., Chicago, Ill.

Eighty-five human hearts were studied at autopsy with particular regard to the pathologic changes in the atria. In fifty-five of these, electrocardiograms were available and a correlation study was made between the anatomical changes and the abnormalities of the auricular deflection. The series included several normal hearts serving as controls. Particular attention was paid to the predominance of anatomical changes in the right or left atrium. No attempt was made to study the specific system. In addition to hypertrophy and dilatation, the main pathologic findings in the atria were different degrees of interstitial fibrosis and coronary arteriosclerosis. Irrespective of the cause, there was a general tendency for the changes to be more marked in the right than in the left atrium. Electrocardiographically, the cases were divided in the following groups, depending on the auricular rhythm and the pattern of the auricular deflection: "within normal limits," "P mitrale," "P pulmonale," auricular fibrillation or auricular flutter, and "non-specific abnormality."

All cases with abnormal auricular deflections in the electrocardiogram showed some degree of anatomical changes in the atria. However, a number of cases with definite anatomical changes in the atria did not reveal any abnormalities of the P wave. Except for a few discrepancies, a close correlation was demonstrated between autopsy findings and specific electrocardiographic patterns.

MALARIA AS A FACTOR IN CARDIAC DISEASE.—J. A. Polanco Billini, M.D., Ciudad Trujillo, Dominican Republic.

Abstract in English not available.

PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA IN WHICH THE MECHANISM IS BASED ON REENTRY.—Reno R. Porter, M.D., and Samuel H. Sandifer, M.D., Richmond, Va.

The case of a 26-year-old white man is presented who had had rapid heart action ever since an attack of "rheumatic fever" twelve years previously. There was no significant incapacity from the tachycardia and no evidence of underlying heart disease. The rhythm was regular for the most part, at which times electrocardiograms showed a supraventricular tachycardia varying in rate from 140 (lying) to 160 (standing). The P waves were low in Lead I and deeply and sharply inverted in Leads II, III, and IV. On occasions the rhythm was irregular, with a rate varying between 52 and 140. Electrocardiograms demonstrated that the irregularity was due to short pauses of varying duration and frequency. These pauses occurred when an abnormal P wave failed to appear or was not followed by a QRS. The pauses ended with a normal sinus beat

which was followed: (1) by another normal sinus beat, (2) by an abnormal P wave, or (3) by an abnormal P wave and resumption of the tachycardia. Study of these tracings demonstrates that the paroxysms of tachycardia are due to a re-entry phenomenon.

The mechanisms of paroxysmal tachycardia are discussed, and the clinical significance of this particular type of tachycardia is pointed out.

SURGICAL DIVISION OF THE PATENT DUCTUS ARTERIOSUS BY MEANS OF A NEW CLAMP.—Willis J. Potts, M.D., Chicago, Ill.

The cardinal points in the diagnosis of a patent ductus arteriosus are reviewed briefly. Unless the murmur is continuous through diastole, the patient very likely does not have an uncomplicated patent ductus arteriosus.

It is generally agreed by cardiologists that the majority of patent ducti should be treated surgically. Whether the ductus should be ligated or cut and sutured has not been decided. Some feel that all ducti should be divided; others think that because of the danger of uncontrollable hemorrhage, multiple ligation is preferable. If the danger of severe hemorrhage from accidental slipping of a clamp could be eliminated, most surgeons would prefer surgical division to multiple ligation with large amounts of foreign material. Although we have ligated twenty-two patent ducti without postoperative complications, it has always been felt that surgical division is a superior procedure.

To obviate the danger of hemorrhage a new clamp has been devised. The principle of the clamp is embodied in a row of very fine teeth in the opposing jaws. The teeth of the clamp, when closed, embed themselves in the adventitia and will not slip, nor will they injure the media or intima. These clamps have been used on nine patients whose ducti have been divided and sutured. There have been no deaths and no operative or postoperative complications.

THE EFFECT OF ACUTELY INDUCED HYPOTHERMIA ON THE CIRCULATORY SYSTEM.—O. Prec, M.D., Prague, Czechoslovakia, R. Rosenman, M.D., Chicago, Ill., and K. Braun, M.D., Jersusalem, Palestine.

Cardiac output was studied by the Fick method and correlated with other changes in the circulatory system during cooling and rewarming. A direct relationship existed between body temperature and oxygen consumption, respiratory, and pulse rates. Cooling induced moderate but consistent decreases of blood pressure. In deeply anesthetized dogs, the cardiac output fell progressively during cooling and initial rewarming, then increasing to only 26 per cent of original values after rewarming. Substantial variations in cardiac output in less deeply anesthetized dogs during early cooling are associated with shivering, increased pulse rate, and oxygen consumption. The cardiac output fell to 35 to 56 per cent of original values at temperature 29 to 27° centigrade. During rewarming the cardiac outputs rose more rapidly and returned almost to basal levels. The vasomotor center was very important in maintaining the blood pressure when the cardiac output decreased. There were large variations in right auricular and pulmonary arterial pressures, but no direct relationship was found between right auricular pressure and stroke volume, pulmonary arterial pressure, and work of the right heart. Associated with cooling were reversible changes in electrical systole, S-T segments, and intraventricular conduction.

FOLLOW UP OF TWENTY-ONE CASES OF SUBACUTE BACTERIAL ENDOCARDITIS AFTER TWO TO MORE THAN FOUR YEARS FOLLOWING RECOVERY.—WALTER S. PRIEST, M.D., AND CHARLES J. MCGEE, M.D., CHICAGO, ILL.

The twenty-one cases are divided into two groups, those (ten) surviving from three to more than four years and those (eleven) surviving from two to three years.

The following points are covered: (a) present work level, (b) incidence of cardiac failure, (c) changes in cardiac size as evidenced by x-ray, (d) development of murmurs not present during the active phase, (e) subsequent episodes of active endocarditis, and (f) relation between duration of active disease before therapy and the present level of cardiac efficiency.

In the first group are three cases of severe decrease in cardiac efficiency or reserve with episodes of cardiac failure. The cardiac efficiency in seven has remained about stationary. All show increase in the heart size as compared with that on discharge from hospital. Signs of valvular involvement not present during the active process have developed in four. Five of the seven showing the best level of cardiac efficiency had a relatively "short" duration of infection before therapy.

The status of the second group is slightly better. This is of doubtful significance since evidence of severe cardiac damage did not appear in the first group until after the third year.

At present our impression is that cardiac damage in this disease is severe in the majority of cases and that ultimate life expectancy is relatively short.

A GENERAL OUTLOOK ON CORONARY DISEASE.—VITTORIO PUDDU, M.D., ROME, ITALY.

The recent progress in the knowledge of the different consequences of coronary disease permits a general outlook of the problem. In this way it is possible to arrange in a progressive series of continuous patterns the pathogenesis (from simple ischemia to complete occlusion) of the functional alterations and anatomical lesions of the myocardium (from the small subendocardial necrosis to massive transmural infarction), their electrophysiopathology, and their clinical pictures. The main steps of this series are: (1) effort angina; (2) prolonged decubitus angina; (3) subendocardial infarction; and (4) massive transmural infarction. From a certain point of view, it is possible to overlook the demarcation line between infarction with and without coronary occlusion: indeed, both mechanisms may overlap.

THIOURACIL IN THE TREATMENT OF HYPERTENSION.—VITTORIO PUDDU, M.D., AND PIER LUIGI GUIDOTTI, M.D., ROME, ITALY.

Hypertensive patients show a frequent increase of the basal metabolic rate and sometimes clinical signs of hyperthyroidism. For this reason the authors tried methylthiouracil in the treatment of hypertension. No other medication was given during the treatment. Up to date, fourteen patients (from 40 to 65 years of age) have been treated. They suffered from uncomplicated hypertension, with initial blood pressure levels over 220/120 and with increased basal metabolic rate. The initial daily dose of the drug of 0.60 Gm. was decreased after three to four weeks to 0.2 to 0.4 Gm. per day. Eleven patients showed definite improvement of the symptoms after the first week of treatment and some of them had a complete disappearance of their complaints some time later. The blood pressure decreased in five of these patients after two to three weeks of treatment. The systolic blood pressure was lowered by 120 mm. Hg in one single

case and by 50 mm. or more in the other four. The diastolic blood pressure was lowered by 20 to 80 millimeters.

Up to date, some of the patients have been under treatment for one year. The discontinuation of the treatment was followed by relapse of the symptoms and signs after three to four weeks. The best results were obtained in patients who showed a good response to cold, posture, and amyl nitrite tests and especially in menopausal hypertension. No signs of intolerance were noted. The studies are being continued.

HYPERTENSION AND TACHYCARDIA DUE TO CONCUSSION OF THE BRAIN.—Wilhelm Raab, M.D., Burlington, Vt.

Published in full, Am. Heart J. **37**:237, 1949.

DIAGNOSTIC ELECTROCARDIOGRAPHIC CRITERIA IN LEFT VENTRICULAR HYPERTROPHY.—Pedro Rabina, M.D., Havana, Cuba.

Abstract in English not available.

ELECTROCARDIOGRAPHIC CHANGES IN TYPHOID FEVER AND THEIR REVERSIBILITY FOLLOWING NIACIN TREATMENT.—

M. Rachmilewitz, M.D., and K. Braun, M.D., Jerusalem, Palestine.

Published in full, Am. Heart J. **36**:284, 1948.

POLYGRAPHIC STUDY OF CARDIAC FIBRILLATION.—Pierre Rijlant, M.D., Brussels, Belgium.

"Intrinsic" variations of the potential at twenty and sixty points of the ventricle of hearts of cats and land turtles were studied at high temperatures of about 30°C. during the ventricular fibrillation as induced by electrical excitation, and simultaneously registered by means of cathode oscillographs which could be controlled by electronic commutators. This did not enable us to demonstrate "circular contractions" in the intact heart. On the other hand, in the turtle heart, the ventricular area of which is injured, fibrillations by circular contraction are easily obtained. The number of leads used at the same time (from twenty to sixty) is not sufficient to exclude completely the possibility that a circular contraction occurred in the maintenance mechanism of the ventricular fibrillation in the intact heart. However, the sudden appearance of activity at the level of an electrode surrounded by a sufficient number of not yet activated electrodes implies that the activity so observed is determined locally; this corresponds either to a local transitory automatism or to a pseudoautomatism maintained by the delayed negativity of the preceding activation. A sufficient definition of the ventricular fibrillation of the mammalian heart can be obtained only by means of a much larger number of leads. We are constructing at present a device making it possible to register 216 leads simultaneously.

SOME OF THE CARDIOVASCULAR MANIFESTATIONS OF EPILEPSY.—J. Manuel Rivero Carvallo, M.D., and Margarita Perrín Chico, M.D., Mexico, D.F., Mexico.

Abstract in English not available.

THE CARDIAC CONDUCTING SYSTEM.—Jane S. Robb, M.D., Syracuse, N. Y.

Using small hearts of various species, including man, serial sections have been cut, stained by Masson's or Mallory's technique, and photographed.

From the photographs outlines have been transferred to plastic, and portions, or all, of the system reconstructed. In the guinea pig the cardiac muscles and their conducting tissue supply have been visualized. In human fetal hearts, the studies are somewhat less completed. The transition of conducting tissue to heart muscle is known for several species. Correlation of such structure to cardiac physiology will be stressed.

THE THEBESIAN VESSELS AND OTHER SMALL VESSELS ON THE HEART AND THEIR ROLE IN NOURISHMENT AND DRAINAGE OF THE MYOCARDIUM.—Joseph T. Roberts, M.D., Little Rock, Ark.

Studies have been made on canine hearts, beating in situ as well as isolated, which indicate that the Thebesian group of vessels can serve as either drainage or nourishment channels for the myocardium of either the left or right ventricles. The direction of flow through these channels depends upon the gradient of pressure between the ventricles and the pressure in the coronary arteries.

By inspection and injection of the Thebesian openings of human hearts it is shown that these channels can be exaggerated in association with slowly progressing coronary artery stenosis.

These experiments suggested an operation, developed initially by the author, to bring a new blood supply to the ischemic myocardium. This consists of anastomosing the coronary sinus with an arterial branch of the aorta. Following such procedures, ligation of coronary arteries was not followed by the usual infarction or death, indicating that this procedure may become of value in the treatment of coronary artery disease with myocardial ischemia.

Attention is also called to the presence of extensive lymphatic circulation in the heart. Studies of the blood supply of the nerves to the heart and relating to a mechanism of cardiac pain and the absence of cardiac pain with cardiac hypertrophy are also reported.

HEART LESIONS IN SOME RHEUMATIC DISEASES NOT INCLUDING RHEUMATIC FEVER; STUDY OF 360 CASES OF RHEUMATOID ARTHRITIS AND 6 OF DIFFUSE SCLERODERMA.—Javier Robles Gil, M.D., Mexico, D.F., Mexico.

Recent histopathologic studies have shown the existence of cardiovascular lesions in rheumatoid arthritis. In this work, the presence of such lesions was investigated clinically in 360 patients. Twenty of these patients (5.5 per cent) presented endomyocardial lesions, as judged by x-ray and electrocardiographic studies. No evidence of rheumatic fever was found. The valvular and endomyocardial lesions were similar to those found in rheumatic fever, with the exception of the high incidence of aortic valvular injury and the great tolerance to the disease. Another 4.7 per cent showed endomyocardial lesions, but with the coexistence of a clinical picture of rheumatic fever. Two and one-half per cent had heart injury due to cardioangiosclerosis, hypertension, or coronary disease. In 3.3 per cent, electrocardiographic changes due to myocardial lesions were found without any other obvious cause but the rheumatoid arthritis. Nine and three-tenths per cent had slight changes in the P waves; and another 5.3 per cent had various electrocardiographic changes, probably due to hypertensive heart disease.

All six patients with diffuse scleroderma showed clinical manifestations of cardiac involvement. In three, globular heart enlargement was found, as revealed by x-ray films. In five, a progressive incomplete bundle branch block was found electrocardiographically. Very likely, eventually it will become a

complete auriculoventricular block, through involvement of both branches, as observed in one case. Two patients died of cardiac insufficiency with bradycardia.

BLOOD PRESSURE AND BODY TEMPERATURE.—SIMON RODBARD, PH.D., CHICAGO, ILL.

Mammals (body temperature 38°C.), including dog, man, rat, and rabbit, have normal diastolic blood pressures averaging about 80 mm. of mercury. Birds (body temperature 42° C.) including chicken, turkey, and duck, have diastolic pressures of about 120 mm. of mercury. Lowering of the body temperature of these animals produces a progressive fall in blood pressure, and rewarming is followed by a return to normal pressures. Similar temperature-pressure relationships have been demonstrated for amphibian (frog) and reptile (turtle). These pressures changes are accompanied by similar changes in heart rate, circulation rate, and cardiac output. However, the temperature-pressure relationship depends on the integrity of the central nervous system, since destruction of the brain eliminates the relationship. Further, blood pressure changes can be demonstrated by thermal stimulation of the brain in the region of the hypothalamus. The significance of these findings is discussed.

CARDIOVASCULAR CHANGES CAUSED BY ARTERIOVENOUS ANEURYSM OF THE THYROID GLAND.—RAMÓN A. ROJAS, M.D., TUCUMAN, ARGENTINA.

Abstract in English not available.

RHEUMATIC DISEASE IN THE ADULT. CLINICAL FORMS, EVOLUTION AND PATHOLOGY.—FRANCISCO ROJAS VILLEGAS, M.D., AND MANUEL BESCAÍN, M.D., SANTIAGO, CHILE.

This work refers to the observation of 200 clinical histories of adult patients hospitalized in an adult medical service for rheumatism and 200 histories of the out-patient rheumatic dispensary. The different clinical forms, degrees of cardiac insufficiency, and the laboratory findings were considered. In the hospital cases which ended in death, the cause of death and the results of the pathological study in every case are given. In the ambulatory cases the evolution of the disease was followed for periods between five and ten years. This evolution is correlated with the type of lesion present, with the degree of radiologic and electrocardiographic alteration, and so forth. There were also studied the different preventive and control measures taken and the various treatments employed.

THE NATURE OF PAROXYSMAL TACHYCARDIA IN ANOMALOUS ATRIOVENTRICULAR EXCITATION.—FRANCIS F. ROSENBAUM, M.D., MILWAUKEE, WIS.

Cases of anomalous atrioventricular excitation raise many considerations not the least of which concerns the nature of the paroxysmal tachycardia which occurs in more than one-half of these patients. Two patients showing unusual features which bear importantly upon this problem have been observed. Observations were made in the first patients at the *onset* of repeated paroxysms as well as when isolated atrioventricular nodal extrasystoles were present. The ventricular complexes during these arrhythmias were of normal form but the P waves were of unusual configuration. It is postulated that the paroxysms arose from a focus in the atrioventricular node so that the manner of activation of the ventricles was normal but the path through the node to the auricles was

blocked. The ventricular impuse reached the auricle by traversing the anomalous bundle. The impulse perhaps returned to the ventricle through the normal pathway, thereby establishing a circus rhythm and initiating a paroxysm. Many isolated extrasystoles followed by retrograde stimulation of the auricles via the anomalous path failed to initiate a paroxysm, apparently because transmission through the normal conduction tissues was blocked. Other isolated extrasystoles were not accompanied by P waves, indicating that retrograde stimulation of the auricles through the accessory pathway occasionally failed. The paroxysm in this patient failed to appear if block occurred in either the normal or the anomalous conduction tissues.

In the second patient observations were made during paroxysmal tachycardia of several days' duration. The patient died suddenly two hours after the paroxysm terminated. The ventricular complexes during both the normal and the abnormal rhythms were bizarre in their configuration. After moderately large doses of quinidine were given partial heart block appeared, although the auricular tachycardia was undisturbed. It may be postulated that in those instances in which the ventricular complexes maintain their abnormal form during paroxysmal tachycardia, the impulse reaches the ventricle from the auricle via the anomalous bundle and therefore spreads over the ventricle in an abnormal manner. To establish a circus movement it must return to the auricles by passing through the normal conducting tissues in a retrograde manner. Such a circus cannot have been present in this patient because it is highly unlikely that both conduction pathways would be blocked at the same instant. It is possible that in this case supraventricular impulses reached the ventricle solely by means of the accessory bundle and that the bundle of His was not functioning. The ectopic focus or the circus rhythm responsible for the paroxysm was then entirely supraventricular in location. When the anomalous bundle became refractory, block occurred and no other functioning pathway was available whereby the impulse could reach the ventricles.

THE HEART IN RHEUMATOID ARTHRITIS; A REVIEW OF RECENT NECROPSY AND CLINICAL INVESTIGATIONS.—EDWARD F. ROSENBERG, M.D., CHICAGO, ILL.

Investigations on this subject which have been conducted during the past decade are reviewed. Necropsy studies based upon an examination of more than 150 cases are summarized. The results indicated that cardiac lesions, which are indistinguishable from those found in rheumatic fever, may be encountered in more than 40 per cent of all patients with rheumatoid arthritis. The lesions encountered have varied in severity, but, in general, have been extensive, often being associated with notable scarring and deformity of valves and with severe myocardial and pericardial lesions. Often this process was responsible for severe heart failure, and frequently, the patients died as a result of the cardiac disease. The heart conditions produced by these lesions were often difficult to detect during life, even in cases where the disease had advanced to a severe degree. Even skilled clinicians often were unable to detect this form of heart disease during life.

A detailed study of the cardiac status of 150 living patients with severe rheumatoid arthritis is also reported. This investigation disclosed evidence of rheumatic heart disease in only 3.4 per cent of the total number of patients studied. The incidence of rheumatic heart disease among a control group was 2 per cent and the difference between the incidence among the patients and the control individuals did not appear to be significant.

The contrasting results from necropsy studies and from clinical examinations are discussed in relation to the possible connection between rheumatic fever and rheumatoid arthritis.

THE FAST SELF-SUSTAINED ACTIVITY OF MAMMALIAN AURICULAR MUSCLE.—A. Rosenblueth, M.D., and J. García Ramos, M.D., Mexico D.F., Mexico.

In isolated auricular appendices, fast nonstimulated discharges follow rapid stimulation after acetylcholine or carbaminoylcholine are administered. The frequency is related to that of the stimuli. Below a critical frequency of stimulation (approximately 20 per second), no automatic discharges ensue. The activity requires the presence of the choline ester. There are more discharges with larger than with smaller doses. Further injections during an episode prolong it. It is longer when acetylcholine is administered after Prostigmine, and longer for carbaminoylcholine than for acetylcholine. Atropine abolishes the phenomenon; curare does not. The discharges end suddenly. The terminal frequency (about 20 per second) is lower than the refractory period requires, for after activity ceases, stimulation elicits faster discharges, which may outlast the stimuli. The activity is usually regular, but may become irregular, as if successive impulses started at different points or several regions were discharging independently. It is probably not maintained by a circus movement; it persists in an area smaller than a square centimeter. It differs from the slow type of self-sustained activity both in frequency and in requiring the presence of an acetylcholine-like agent which inhibits the slow activity.

NORMAL VALUES OF THE ARTERIAL PRESSURE AND FREQUENCY OF ARTERIAL HYPERTENSION IN HIGH ALTITUDES.—Andres Rotta, M.D., and Artemio Miranda, M.D., Lima, Peru.

In a town of about 7,000 inhabitants and at 13,850 feet above sea level (Morococha, Peru), an investigation was conducted to detect cases of arterial hypertension. At the same time the blood pressure of 1,878 healthy individuals between 18 and 71 years of age was measured. Among this group there were fifty-three Caucasians (North Americans, Italians, Spaniards, and Peruvians), dwellers of high altitudes for many years; the rest were native Indians.

The following results were found:

1. Neither in the investigation nor in the direct examinations were cases of arterial hypertension found.
2. The systolic arterial pressure is lower in men at high altitudes than in those at sea level, (mean pressure, 108 mm. Hg); the diastolic arterial pressure is higher than at sea level, (mean pressure, 88 mm. Hg).
3. Since the few nonIndians showed no difference from the natives, either in the systolic or in the diastolic pressure, it may be concluded that the figures obtained have nothing to do with the racial characteristics and that chronic anoxia does not influence arterial pressure.

THE SYSTOLIC EXPANSION OF THE LEFT AURICLE IN MITRAL DISEASE.—D. Routier, M.D., and R. Heim de Balsac, M.D., Paris, France.

The radiologic examination of patients with mitral disease permits recognition in the most advanced cases of an expansion of the left auricular contour during ventricular systole. Radiokymography gives more precise information regarding this phenomenon, which can be observed either in the anteroposterior position when the left auricle extends to the right border of the heart, or in the right anterior oblique, left lateral, or left posterior oblique position, when the filled esophagus follows the auricular outline closely. A description is given of the radiokymogram and of the expansion observed. *Interpretation:* The left auricular distension during ventricular systole is evidence of auriculoventri-

cular regurgitation or "mitral insufficienty"; thus this physiopathological disturbance can be easily demonstrated during life. Our radiological-clinical study of the phenomenon is based upon several hundred observations.

Left auricular systolic expansion becomes more marked with marked enlargement of the left auricle and in the presence of auricular fibrillation; the more advanced the cardiac lesion, the more marked is the systolic expansion of the left auricle. The auricular expansion may or may not be present with stenosis or an apical systolic murmur of mitral insufficiency. The different possibilities can be explained by the volume of regurgitating blood. If regurgitation is slight it may set into vibration the mitral apparatus and produce a murmur but may be insufficient to distend the auricle. On the contrary, if it is marked it may distend the auricle without causing a vibration of a mitral apparatus which is more or less rigid, thickened and gapping.

The left auricular systolic expansion not only establishes the diagnosis of mitral insufficiency, but permits appreciation of the importance of that regurgitation. Thus, it is a sign of considerable importance both physiopathologically and clinically.

CARDIOVASCULAR STUDIES, WITH FOLLOW-UP RESULTS, OF THE VICTIMS OF THE TEXAS CITY DIASTER.—ARTHUR RUSKIN, M.D., GALVESTON, TEXAS.

As previously reported (Am. J. Med. **4**: 228, 1948) elevated diastolic blood pressure peaks of 95 mm. or over were found in the majority of 180 hospitalized patients injured by the Texas City explosions of April 16, 1947. This incidence of acute hypertension, occurring especially from two to twenty-eight hours following the blasts, is much higher than that found in hospitalized surgical patients or in various battle zones during World War II.

Some four to seven months following the explosions, 111 cases were reexamined for signs of cardiovascular disease. It appeared that 23 per cent of the cases showed diastolic blood pressures of 95 mm. or over, even though the lowest readings obtained following rest were so evaluated. While statistically valid comparable figures for the local general population are not available, the figure of 23 per cent was found to be statistically higher than the available figure either of industrial examinees or of insurance applicants.

Cold pressor tests were positive in 72 per cent of the postexplosion group and in 77 per cent of the follow-up group of blast victims.

In addition to the finding of hypertension as a possible result of the blast, we saw a case of severe hypertensive reaction following massive pulmonary embolism. Some cases of possible cardiac blast injuries, proved pathologically, were also encountered. Complete studies, including electrocardiographic and other examinations, throw some light upon the possible etiology of the cardiovascular abnormalities.

THE EFFECT OF VASOCONSTRICTIVE AND HYPERVOLEMIC MEASURES UPON TETRAETHYL AMMONIUM ORTHOSTATIC HYPOTENSION.—ARTHUR RUSKIN, M.D., GALVESTON, TEXAS.

We have previously reported a finding of orthostatic hypotension in various clinical states in which vasodilation seemed to play a prominent part (Proc. Am. Fed. Clin. Res. **3**: 44, 1947). Among the conditions previously and recently observed to be associated with orthostatic hypotension of various degrees have been acute and severe chronic anemias, other blood dyscrasias, hyperthyroidism, and alcoholism. Both ephedrine and desoxycorticosterone were observed by us to prevent in various degrees the orthostatic phenomona.

Tetraethyl ammonium uniformly produced orthostatic hypotension in

doses of 0.2 Gm. to 0.5 Gm. intravenously. In many cases we observed relative hypertension in the recumbent position, a phenomonon also often observed in clinical orthostatic hypotension. With a dose of 0.5 Gm. the effects were pronouncedly less or gone within thirty minutes in the majority of cases. Tetraethyl ammonium decreased the circulating blood volume (Evans blue method). While preliminary injections of paredrine (30 to 60 mg.), ephedrine (50 mg.), plasma (750 to 1,000 c.c.), and desoxycorticosterone (20 to 40 mg., plus 10 Gm. of sodium chloride) tended to increase the blood pressure, particularly in the recumbent position, subsequent tetraethyl ammonium injections produced variable results. In some cases orthostatic hypotension and tachycardia were prevented, in others they were not. Paredrine and ephedrine were effective in preventing orthostatic syncope and alleviating orthostatic hypotension in seven out of ten cases; plasma and desoxycorticosterone, in a minority of cases. The drops in circulating blood volume following tetraethyl ammonium were prevented in some cases, particulary by preliminary Paredrine and plasma. As in clinical cases, venous pressures and circulation time in the recumbent and upright positions were apparently not affected by Stamon orthostatic hypotension short of syncope.

HISTOLOGICAL CHANGES IN EXPERIMENTAL RHEUMATISM (ANAPHYLATIC).—M. Salazar Mallén, M.D., Isaac Costero, M.D., and Elena Lozano, Q.B.P., Mexico, D.F., Mexico.

Previous studies of De Gortari, Pellón, Costero and Barroso Moguel have shown that in rheumatic patients there exist encephalic lesions which give rise to clinical and anatomic manifestations described as a true rheumatic encephalopathy.

Since there are not experimental investigations related to the histologic features in the brain in experimental allergic rheumatism, the authors proceeded to sensitize rabbits with horse serum and to provoke the allergic shock through intravenous and intra-articular injections of antigen four weeks later. Seventy-two hours after the shocking dose, microscopic study of the brain revealed histologic lesions in some of the animals that could be readily compared with those already observed in cases of rheumatic encephalopathy in man.

Since none of the rabbits that were not shocked displayed these changes, it is concluded that there is experimental rheumatism. This gives support to the belief that rheumatic fever in its general pathological picture, as well as in the participation of the central nervous system, belongs to a general process of allergic sensitization, with anatomicopathologic changes, in man as well as in the animal, of the microglial component of the nervous tissue.

ATROPHY OF THE HEART; CLINICAL, PATHOLOGICAL, ELECTROCARDIOGRAPHIC CORRELATION IN 85 PROVEN CASES.—D. Santiago-Stevenson, M.D., San Juan, Puerto Rico, and H. K. Hellerstein, M.D., Cleveland, Ohio.

Eighty-five cases of atrophy of the heart were encountered in 2,000 consecutive autopsies. Forty-four had brown atrophy, with characteristic bipolar pigment deposition, and an average weight of 231 grams. Forty-one had simple atrophy, devoid of pigment, with an average weight of 202 grams.

The following features were noted:

1. The incidence was three times greater in women than in men, as compared with autopsy population. The average age of the brown atrophy group was 61.7 years; of the simple atrophy group, 41.8 years.

2. The ratio between heart weight and body weight was 0.42 per cent in brown atrophy and 0.48 per cent in simple atrophy (normal, 0.43 to 0.40 per cent).

3. All but one case showed extreme wasting with generalized atrophy. Major clinical diagnoses included neoplasms, chronic infections, and degenerative and metabolic diseases.

4. Important factors in production of emaciation were prolonged illness, bedfastness, fever, surgical procedures, radiation, and gastrointestinal dysfunction.

5. Clinically the atrophic heart was small or of normal size, quiet, inactive, with a faint apical or precordial short systolic murmur in 25 per cent of the cases.

6. Characteristic electrocardiograms showed progressive diminution of voltage of P, QRS, T wave, and prolongation of Q-T intervals.

7. Blood pressure fell in 76.4 per cent of cases; normotension to low levels, and hypertension to normal or hypotensive levels.

8. The small heart was able to bear its load, as shown by the low incidence of clinical heart failure. Only three patients had clinical and pathological evidence of heart failure and they had concomitant organic heart disease.

THE RECIPROCAL ACTION OF WATER, SODIUM, AND ACIDS IN RESISTANT CARDIAC EDEMA.—F. R. SCHEMM, M.D., GREAT FALLS, MONT.

Cardiac edema in advanced disease which was resistant to more usual measures was cleared in 80 per cent of 322 instances by the institution of a regimen which included a large intake of water, a moderate restriction of sodium, and small amounts of acid. In 160 instances edema did not clear with only two of the three factors of the regimen in force until the third factor was added; this was noted in from fifty to sixty instances for each of the three factors. In these observations water was given in amounts of from 1,500 to 8,000 c.c. daily, sodium was restricted to from zero to 1,200 mg. daily, and acids were given as diet or drugs, including ammonium chloride by vein, in amounts the equivalent of from zero to 16 Gm. of ammonium chloride daily.

From these observations, it seems apparent that each factor of the regime has its limitations as well as uses and the importance of their reciprocal action emerges. The most severe restriction of sodium alone, the most extreme forcing of water alone, the heaviest doses of acid alone, or the combination of any two of these, may leave untouched a resistant edema which is capable of responding dramatically to the reciprocal action of all three factors, even when each is enforced to a much less drastic degree.

MECHANISM OF AURICULAR FLUTTER AND FIBRILLATION.—D. SCHERF, M.D., NEW YORK, N. Y.

Published in full, Am. Heart J. **36**:241, 1948.

THE EFFECT OF ERGOTAMINE PREPARATIONS ON THE ELECTROCARDIOGRAM.—D. SCHERF, M.D., AND M. SCHLACHMAN, M.D., NEW YORK, N. Y.

It has been claimed that the injection of ergotamine tartrate prevented the occurrence of postural inversion of the T waves (Nordenfelt) and that inverted T waves which may occur in the supine position in the emotionally tense individual or in neurocirculatory asthenia may be normalized by this drug (Wendkos). Both authors suggested that ergotamine tartrate could be utilized to differentiate a "functionally" inverted T wave from an inversion caused by organic disease.

Twelve patients studied by us showed significant changes in the T waves on assuming the erect position. When the experiment was repeated after the intravenous injection of ergotamine tartrate, the positional inversion of the

T waves was not prevented from recurring in eleven cases. Nineteen patients who had organically inverted T waves because of left ventricular strain and/or organic heart disease were given an intravenous injection of 0.5 mg. of either ergotamine tartrate of dihydroergotamine 45. Seven of these patients exhibited a normalization of the T waves. Five patients developed severe anginal pain which lasted from two to twelve hours, and one of these patients who had syphilitic aortitis with narrowing of the coronary ostia died twelve hours after the injection.

From these observations, it is concluded that ergotamine preparations will not invariably prevent the inversion of the T waves with a change of position of the patient. Ergotamine preparations can cause a normalization of organically inverted T waves and therefore cannot be used as a diagnostic test. Their use is dangerous in patients with coronary artery disease.

CLINICAL OBSERVATIONS WITH FAGARINE.—D. SCHERF, M.D., A. M. SILVER, M.D., AND L. D. WEINBERG, M.D., NEW YORK, N. Y.

Fourteen injections of alpha-fagarine hydrochloride were given to thirteen patients with various forms of tachycardias, auricular flutter, and auricular fibrillation. The dose varied between 0.05 and 0.12 gram. In six patients the existing arrhythmia disappeared promptly after the injection. In two patients, however, fatal ventricular fibrillation appeared; in three others dangerous multifocal ventricular extrasystoles were observed.

The observations and side reactions in all cases are discussed and the risk involved in the use of this drug is stressed.

ETIOLOGY OF AURICULAR FIBRILLATION AND THE MECHANISM OF ITS PERPETUATION.—J. G. SCHLICHTER, M.D., CHICAGO, ILL.

In this report, our experience in man and dog relating to the etiology of auricular fibrillation and the mechanism of its perpetuation is presented. Vagal stimulation and anoxia are the main etiological factors in the initiation and perpetuation of auricular fibrillation.

Vagal stimulation (mechanical and chemical) may induce auricular fibrillation. Acetylcholine injected directly into the blood stream was used in our experiments to produce chemical vagal stimulation. Moderate anoxia reduces the threshold of the auricles to the initiation of fibrillation, but does not induce this arrhythmia, per se; marked anoxia, on the other hand, increases the threshhold to fibrillation.

Anoxia of the auricles was found or produced: (1) by interference with or obstruction of its vascular supply, (2) by a decrease in the amount of oxygen carriers, (3) by a decreased oxygen content of the blood due to anoxic anoxemia, and (4) by interference with tissue respiration.

The relationship between vagal stimulation and anoxia can be plotted in a graph, and on this correlation, the cause of the perpetuation of auricular fibrillation can be demonstrated. The clinical implication of these findings and the therapeutic approach to this problem are illustrated and discussed.

CARDIOVASCULAR CHANGES IN PERNICIOUS ANEMIA BEFORE AND AFTER THERAPY.—STEVEN O. SCHWARTZ, M.D., AND VLADIMIR C. FLOWERS, M.D., CHICAGO, ILL.

Ninety-two patients with pernicious anemia, ranging in age from 35 to 81 years, and equally distributed between the sexes, were studied while in hematologic relapse. Of these sixty-nine were Caucasian and twenty-three were Negro. Fifty-five complained of dyspnea, thirty-one of edema, eight had angina

pectoris, and one had intermittent claudication. Fifty-nine had systolic murmurs, distributed as follows: apical, thirty; pulmonic, ten; aortic, six; diffuse, thirteen. One patient had an apical diastolic murmur which disappeared on liver therapy (this patient had hypertension). Only eighteen patients had blood pressures over 150/90 while in relapse. Seventy-two of the patients had electrocardiograms taken; of these, forty-four were interpreted as abnormal. Fifty-seven patients had their cardiac size determined by x-ray films, thirty being found normal.

Forty-four patients were re-examined when blood values had returned to normal (three months). Of these, eleven had systolic murmurs (five apical, five aortic, one pulmonic), while nineteen had hypertension (150/90 plus). Electrocardiograms revealed abnormalities in twenty of forty-one repeat studies. Cardiac size was found to be normal in twenty-five of thirty-seven patients re-examined.

Discussion will center on the interpretation of these findings as it relates to: (1) the criteria of diagnosing cardiovascular disease in the presence of severe anemia; (2) the significance of the findings when reinterpreted on the basis of the age group involved in the study; and (3) the influence of the rapidity of onset of the anemia on the symptoms and findings.

CARDIOVASCULAR SYPHILIS IN YOUNG WHITE MALES.—JOHN B. SCHWEDEL, M.D., AND KONA SIMON, M.D., NEW YORK, N. Y.

Five hundred ninety-five syphilitic men and 786 controls were examined for auscultatory and radiographic findings to determine the incidence of aortic dilatation, aortic insufficiency, and a combination of aortic dilatation plus aortic systolic murmur and/or accentuation of the second aortic sound. The average incidence of dilated aorta was 4.2 per cent in the controls and 18 per cent in the syphilitic group. Ausculatory findings were three times as frequent in the syphilitic group without aortic dilatation and twice as frequent when the aorta was dilated. Isolated aortic insufficiency was present in 7.2 per cent.

Criteria for the diagnosis of syphilitic aortitis are suggested consisting of the presence of dilated aorta combined with significant auscultatory findings. The presence of a dilated aorta in syphilitics below the age of 40 years in the absence of aortic insufficiency, plus aortic systolic murmur or accentuation A_2, is sufficiently frequent to warrant the presumptive diagnosis.

Radiographic and fluoroscopic criteria, consisting chiefly in increased arching in the posteroanterior and left anterior oblique views, are illustrated.

PARCHMENT HEART (OSLER).—HAROLD N. SEGALL, M.D., MONTREAL, CANADA.

In revising the sixth edition of his textbook, *The Principles and Practice of Medicine*, Osler introduced the following paragraph in the chapter on dilatation of the heart: "Dilatation may be chronic, in which case it is associated with hypertrophy. Not always, however; there is an extraordinary heart in the McGill College Museum showing a parchment-like thinning of the walls with uniform dilatation of all the chambers; in places in the right auricle and ventricle only the epicardium remains." Periodic long searches of medical literature were made in the past few years and no reference to a similar case of dilatation and generalized thinning of the myocardium could be found. This unique specimen represents a condition about which one can only speculate in considering the etiology and pathologic physiology. The records of the McGill Museum contain no clue to the patient's history in this case. It is significant that neither the heart valves nor the myocardium reveals any evidence of inflammatory disease

and that the coronary arteries are normal. The theoretical question, what degree of dilatation without hypertrophy may be reached by myocardium?, is answered by this heart more effectively than by any known experimental technique, or by any other clinical observation.

Illustrations as well as the specimen, which at first glance resembles a distended ovarian cyst, will be shown.

THE DIFFERENT TYPES OF INTRAVENTRICULAR BLOCK.—MARCEL SEGERS, M.D., BRUSSELS, BELGIUM.

Published in full, Am. Heart J. **37**:92, 1949.

COARCTATION OF THE AORTA.—MORSE J. SHAPIRO, M.D., MINNEAPOLIS, MINN.

The subject of coarctation of the aorta has assumed practical significance now that this abnormality can be cured by surgical intervention. It seemed important, therefore, to examine the data on twenty patients observed over a period of several years. From this study the following information has been obtained:

1. The diagnosis is frequently missed.
2. Follow-up studies revealed a gradual increase in blood pressure with an accompanying increase in size of the left ventricle. The extent of erosion of the ribs, where this sign is present, increases.
3. Erosion of the ribs is not always present.
4. There is no clear correlation between rib erosion, size of the left ventricle, and degree of constriction of the aorta.
5. Collateral circulation does not develop if an accompanying patent ductus arteriosus of good size is present.
6. Enlargement of the left subclavian artery, as revealed by x-ray films, is frequently a helpful diagnostic sign.
7. Four cases observed during surgical intervention and three at postmortem examination will be discussed in detail.

BIOLOGIC STANDARDIZATION OF DIGITALIS PRODUCTS BY MEANS OF THE GUINEA PIG METHOD: COMPARISON WITH THE CAT METHOD; DIFFERENCES AND ADVANTAGES.—EUGENIO D. DA SILVA CARMO, M.D., RIO DO JANEIRO, D.F., BRAZIL.

Abstract in English not available.

MOVEMENTS AND SOUNDS OF THE HEART VALVES OF VARIOUS LABORATORY ANIMALS (MOTION PICTURE WITH SOUND RECORDINGS).—H. L. SMITH, M.D., E. J. BALDES, M.D., AND HIRAM E. ESSEX, M.D., ROCHESTER, MINN.

The hearts of various laboratory animals were perfused with oxygenated Ringer-Locke solution and were kept beating for various periods of time. Openings were made in the different chambers of the hearts and motion pictures were made of the movements of the mitral, tricuspid, aortic, and pulmonic valves. Sound recordings and electrocardiographic tracings were made at the same time.

X-RAY KYMOGRAPHY IN THE DIAGNOSIS OF PATENT DUCTUS ARTERIOSUS.—K. SHIRLEY SMITH, M.D., AND FRANKLIN G. WOOD, M.D., LONDON, ENGLAND.

In the present study x-ray kymography has been applied to the diagnosis of patent ductus arteriosus. It is considered that the radiokymographic appearances which we now present are characteristic and diagnostic of this congenital abnormality.

In kymograms of the normal heart taken by the moving grid technique the left border of the cardiac silhouette is made up of four zones which merge one with another. In patent ductus arteriosus we have observed three additional features. (1) *Vibration waves.* These are situated immediately below the aortic zone and between this and the pulmonary zone, and suggest a visual radiological counterpart of the palpable clinical thrill. (2) *Para-aortic waves.* These lie parallel to and lateral to the aortic zone and are usually faint. They differ from the faint zig-zag shadows often seen well away from the mediastinum and due simply to transmitted pulsation from the aorta or left ventricle. (3) *Exaggerated pulmonary artery waves.* These are an amplification of the waves normally seen in this zone of the pulmonary artery.

X-ray kymograms have been made in fourteen consecutive patients proved to have patent ductus arteriosus. In spite of the difficulties of radiography in young children, vibration waves were seen in all but two cases. Para-aortic waves and exaggerated pulmonary artery waves were observed less frequently, but there was only one patient in whom none of these kymographic signs was found.

CONTRIBUTION TO THE STUDY OF THE WOLFF-PARKINSON-WHITE SYNDROME BY THE INTRACAVITY LEADS.—Jorge Soberón Acevedo, M.D., Demetrio Sodi Pallares, M.D., Pablo Thomsen, M.D., Bernardo L. Fishleider, M.D., and Antonio Estandía Cano, M.D., Mexico, D.F., Mexico.

The intracavity potential was studied in the right chambers of the heart in six patients with the Wolff-Parkinson-White syndrome. In relation to the morphology of the intracavity tracings, it was possible to classify the cases under study into two main groups. *Group A:* ventricular complexes of the QS type with a positive T wave with the electrode in the region near the pulmonary conus, and purely positive complexes with a negative T wave and with the intrinsic deflection 0.08 second after the onset when the electrode was near the tricuspid valve. *Group B:* ventricular complexes of the QS type with a positive T wave near the tricuspid valve, and purely positive complexes with a negative T and with the intrinsic deflection 0.08 seconds after the onset with the electrode near the pulmonary conus. By producing septal extrasystoles, we obtained intracavity tracings similar to those we have described.

In dogs, the experimental excitation of the ventricular septum in regions near the pulmonary conus and the tricuspid valve induced ectopic, self-sustained rhythms which at times resembled the typical pattern the syndrome produces in man.

We advance the theory that the Wolff-Parkinson-White syndrome may be caused by the presence of an anomalous atrioventricular conduction through a congenital bundle which ends in certain hyperexcitable zones of the septum situated near the pulmonary conus for the cases classified as Type A, and near the tricuspid valve for those of Type B.

EXPERIMENTAL AND CLINICAL ELECTROCARDIOGRAPHIC STUDY OF INCOMPLETE BUNDLE BRANCH BLOCK.—Demetrio Sodi Pallares, M.D., Pablo Thomsen, M.D., Ennio Barbato, M.D., Jorge Soberón Acevedo, M.D., Bernardo L. Fishleder, M.D., and Antonio Estandía Cano, M.D., Mexico, D.F., Mexico.

Experimental Aspect in Dog.—Transitory bundle branch block is produced by piercing the ventricular wall and pressing on the septum with a probe at the site of emergence of the branches of the bundle of His. On disappearance of the block there follow a number of different transitional complexes representing

incomplete block. A study of these transitional complexes was made with auricular and ventricular intracavity leads, and with epicardial, unipolar, and standard limb leads. Ventricular intracavity leads register a tracing of the RS type when there is complete homolateral bundle branch block. In the transitional complexes, R diminishes and S increases gradually to normal. As the block increases, epicardial leads give essentially positive complexes with initial slurring referable to abnormal septal activation, since it is synchronous with an intracavity positivity.

Clinical Electrocardiographic Aspect.—Electrocardiograms suggestive of incomplete block are shown. Q is missing in Leads I, V_L, V_5, and V_6 in left incomplete block; the slurring is as characteristic as in experimental tracings. V_1 is very characteristic in right incomplete block. rsRS type complexes are always very suggestive. The diagnostic significance of the duration of QRS is minimal.

The intraventricular study of a patient with right bundle branch block showed the following: upon swallowing, there appeared varied transitional forms of incomplete block. The complexes are of the rsrS, rsrs, and rsr (embryonic) S types. A complete set of precordial leads were also taken.

HYPERPROTEINEMIA IN HEART FAILURE.—Ben Sommers, M.D., St. Paul, Minn.

Four cases of women with chronic right heart failure over a period of years are presented. Tricuspid insufficiency was an associated lesion in all cases. Venous pressures were constantly elevated and generalized anasarca was a prominent symptom in all. Disappearance of the edema occurred spontaneously in all cases, and its disappearance was shown to be due to the development of hyperproteinemia. Osmotic pressure determinations, liver biopsies, and autopsy in two cases are presented. The etiology of cardiac edema is discussed.

A NEW STAIN FOR URINARY SEDIMENTS: ITS VALUE IN THE DIFFERENTIAL DIAGNOSIS OF HYPERTENSION.—Richard Sternheimer, M.D., and Barney I. Malbin, M.D., Chicago, Ill.

Urinary sediments may be stained by adding to the wet sediment one drop of a mixture consisting of alcoholic solutions of safranine 0 and crystalviolet in proportions of 97 parts and 3 parts, respectively. Epithelial cells, leucocytes, and casts stain readily, whereas erythrocytes either do not stain or stain only faintly. Thus, in cases of marked hematuria, the presence of epithelial cells, casts, or pyuria can be discovered easily. Recognition of hyaline, granular, epithelial, pus, and red cell casts is greatly simplified by the stain.

Two types of leucocytes may be differentiated: (1) violet staining, dead cells of uniform size and typical nuclear structure, commonly occurring in chronic cystitis, prostatitis, and vaginal discharge; and (2) faintly blue staining, usually larger cells, varying in size, containing one to four spherical nuclei. When studied with oil immersion lens, these latter leucocytes show marked Brownian movement of the cytoplasmic granules, a phenomenon described in fresh, degenerating leucocytes. Cells with Brownian granular movements are present in acute cystopyelitis, abscess of kidney or prostate, and particularly in advanced pyelonephritis. They are uniformly absent in essential hypertension not complicated by inflammatory renal disease.

On the basis of these observations, now extending over two years, a correct diagnosis of pyelonephritis in advanced cases of hypertension was made in twelve cases confirmed by autopsy. In one case, pyelonephritis superimposed upon an existing glomerulonephritis was diagnosed clinically and verified by autopsy.

STUDIES IN HEART BLOCK AND AURICULAR FIBRILLATION.—ADOLPH SURTSHIN, M.D., AND LOUIS HORLICK, M.D., CHICAGO, ILL.

Acetylcholine injected intravenously in dogs and man may produce A-V block and auricular fibrillation. In thirty-one dogs, the minimal amount of acetylcholine necessary to produce second degree A-V block was determined. Doses of ten and twenty times this amount were then administered and the resulting arrhythmias recorded electrocardiographically. The dogs were then made anemic either by repeated bloodletting or by the exhibition of either of two hemolytic agents, acetylphenylhydrazine and *n*-propyldisulfide, and the standardizations repeated. In control standardizations the minimal standard dose was found to vary widely among different animals, but to remain relatively constant for the same animal. During each of the three types of anemia produced, the minimal standard dose fell markedly in a manner roughly paralleling the hemoglobin level. An increased tendency to fibrillate also developed during anemia. The development of auricular fibrillation was preceded in almost every instance by the development of intra-auricular block and A-V block. On a number of occasions fibrillation of the auricles clearly began with polyphasic P waves of unusual contour, suggesting that auricular re-entry is the mechanism of the genesis of auricular fibrillation. The increased sensitivity of the heart in anemia to acetylcholine (vagal stimulation) is probably due to anoxemia of the myocardium.

THE TREATMENT OF ARTERIAL HYPERTENSION WITH DIHYDROERGOCORNINE METHANESULFONATE (D.H.O. 180).—RALPH M. TANDOWSKY, M.D., AND FRED V. CERINI, M.D., LOS ANGELES, CALIF.

Dihydroergocornine methanesulfonate, an ergot alkaloid, has known sympathicolytic properties in small dosage. Its action is based on functional blockage of sympathetic impulses to the arteriolar stream bed. Because of its cumulative properties, it must be given with caution as cumulation frequently agitates the hypertensive state. Known hypertensives appear to be hyperreactive to this alkaloid.

This preliminary report constitutes a study of an unslected group of sustained hypertensive patients whose basal, untreated blood pressure level was determined by prolonged observation prior to the administration of the alkaloid. The drug was given daily by the intravenous route in dosage ranging from 0.1 to 0.5 mg. until the ideal basal treated pressure was obtained. During this period careful clinical observation was made to determine the ideal clinical arterial pressure level for each subject. If results proved satisfactory, the drug was then administered orally in liquid form each day (0.25 to 0.5 mg.) for maintenance.

Preliminary studies seem to indicate that dihydroergocornine may prove to be a valuable adjunct in the palliative treatment of hypertension. Because of its action on the high autonomic centers in the medulla and hypothalamus, a sustained action can be depended upon, an action unlike that of the vasodepressor drugs now in common use.

THE BEHAVIOR OF THE ELECTRICAL SYSTOLE (QT INTERVAL) IN RHEUMATIC DISEASE IN CHILDREN.—Leo M. Taran, M.D., and Nelly Szilagyi, M.D., Long Island, N. Y.

In recent months there has been some discussion in the literature with regard to the value of the measurement of the electrical systole in rheumatic carditis. The prolongation of the electrical systole (Q-T interval) has been proposed as one more diagnostic sign for rheumatic carditis.

The duration of the electrical systole (Q-T interval) has been studied in a group of rheumatic children over a long period of time. It has been noted that rheumatic patients fall into five classes in regard to the duration of the Q-T interval: (1) Patients who show a normal Q-T interval which remains unaltered during the entire period of observation. (2) Patients who show a normal Q-T interval which becomes prolonged during the period of observation. (3) Those who come under observation with a prolonged Q-T interval which becomes normal. (4) Those who have a slightly prolonged Q-T interval which remains constant for long periods of time. (5) Those who have moderately prolonged Q-T interval which either remains unaltered or becomes markedly prolonged during the period of observation.

The evidence points up the observation that the prolongation of the electrical systole (Q-T interval) in rheumatic patients is a helpful diagnostic test for the presence of rheumatic carditis and in addition seems to be of important prognostic significance in following the course of acute rheumatic heart disease.

FEVER IN MYOCARDIAL INFARCTION.—Herman Tarnower, M.D., Scarsdale, N. Y.

The importance of fever in acute myocardial infarction has never been fully appreciated. No similar analysis is to be found in the literature. The basis for this study was one hundred consecutive cases of myocardial infarction. A rather typical latent period and temperature curve may be expected in over 95 per cent of those who survive the first twenty-four hours. The height and duration of the fever were analysed as to their prognostic significance, and correlated, as far as possible, with autopsy findings. Charts have been prepared to demonstrate these factors. Necropsy material served to show how little myocardial damage is required to produce a temperature elevation. Several cases illustrated the necssity for taking rectal rather than mouth temperatures. There were several interesting clinical and electrocardiographic findings noted in the afebrile cases.

Though fever is a well-known sign in this disease, its significance has never been properly emphasized. The general practitioner rarely considers it important enough to have frequent, careful, rectal temperature recordings. He is more likely to rely solely on the electrocardiogram for confirmation of his diagnosis. Several of our cases demonstrated the fact that electrocardiographic changes may not appear for two or more weeks after the acute episode. In these instances, the history and typical temperature curve may give one confidence to persevere until electrocardiographic evidence appears.

The relative diagnostic value of the various clinical and laboratory signs employed in myocardial infarction is evaluated.

COMPLETE TRANSPOSITION OF THE AORTA AND A LEVOPOSITION OF THE PULMONARY ARTERY; CLINICAL, PHYSIOLOGICAL, AND PATHOLOGICAL FINDINGS.—Helen B. Taussig, M.D., and Richard J. Bing, M.D., Baltimore, Md.

Presented in full in this issue.

QUANTITATIVE PRODUCTION OF MYOCARDIAL NECROSIS WITH ELECTROCARDIOGRAPHIC ANALYSIS.—C. B. Taylor, M.D., O. H. Akre, M.D., and C. B. Davis, Jr., M.D., Chicago, Ill.

A new method has been used in producing myocardial lesions resembling infarcts in the hearts of dogs. The heart is exposed surgically and a hypothermal instrument is applied to the epicardium. Lesions having desired dimensions are then produced by controlled cooling of the adjacent myocardium. Lesions are reproducible in successive animals in the walls of the auricles and ventricles and in the interventricular septum. Variations such as those encountered in producing experimental infarcts by arterial ligation do not occur.

Serial electrocardiographic tracings, using standard limb leads and varied precordial leads, were obtained at intervals after the production of lesions. Animals were sacrificed after stabilization of electrocardiographic patterns. The size of each lesion in relation to cardiac size and its location were determined. Data obtained from standard limb leads and varied precordial leads were correlated with the location, age, and size of lesions. Accurate prediction as to size, location, or age of lesions produced was not possible. Precordial leads localized early anterior lesions to the right or left ventricle. Posterior ventricular lesions were distinguishable from anterior or apical ventricular lesions. Certain septal lesions gave the characteristic changes of bundle branch block.

NEW TECHNIC FOR THE RAPID PRODUCTION OF A HEART-LUNG OR HEART-LUNG-ORGAN PREPARATION.—Teodoro Texidor, M.D., Chicago, Ill.

This technique is based on the introduction of a Pyrex cannula into the descending aorta to occlude its branches. The advantages of the procedure are as follows:

Opening the thorax is practically bloodless since the intercostal vessels are interrupted. The circulation of the organ to be perfused is never interrupted; this is important, especially for the liver, where the slightest oxygen deficiency rapidly breaks down the glycogen.

The animal (dog) is first anesthetized and heparinized. The trachea is cannulated. A mid-line incision is made from xiphoid to pubis to expose the abdominal aorta. A strong cord is passed behind it one inch above the bifurcation and is loosely tied. An arterial clamp is placed one inch above the ligature and locked. The aorta is incised near the bifurcation, and the cannula is introduced upward until it reaches the clamp which is then released and the cannula rapidly pushed forward to the arch. The ligature is then quickly tied. Artificial respiration is initiated, the ribs cut, and the breastplate lifted, exposing the mediastinum and lungs. Another cord is ligated around the aorta near the arch, including the upper end of the cannula. The brachiocephalic vessels, azygos vein, and inferior cava are then ligated.

THE ELECTROCARDIOGRAM IN CONGENITAL HEART DISEASE.—MILTON H. UHLEY, M.D., CHICAGO, ILL.

A study was made correlating the electrocardiographic findings and congenital heart lesions, proved by autopsy, in a series of fifty-three cases. The records are divided into "specific" and "non-specific" pattern groups. It is pointed out that recognition of heart strain patterns is significant in identifying certain congenital lesions.

The "*specific*" *pattern group*, in infancy and early childhood, includes the following lesions: (1) Dextrocardia, which shows the classical inversion of all the components of Lead I. (2) Left coronary artery arising from the pulmonary artery, which produces a picture resembling the adult anterior wall infarction or anterior wall type of coronary insufficiency. (3) Von Gierke's Disease, which presents a picture of combined heart strain. (4) A group of lesions producing left heart strain patterns: (a) those affecting the systemic outflow tract, as aortic and subaortic stenosis; possibly congenital bicuspid aortic valve; coarctation of the aorta, adult type; congenital stenosis of the isthmus of the aorta. (Aortic atresia with underdeveloped left ventricle and aplasia of the mitral valve and ring does not belong to this group; it produces right axis shift or right heart strain. (b) Anomolies of the tricuspid valve as: tricuspid atresia with under developed right ventricle; and Ebstein's disease, congenital downward displacement of the tricuspid valve. (c) Truncus arteriosus communis. (d) Single ventricle with its variant associated anomalies.

The "*non-specific*" *patterns* presented and discussed are: (1) Right heart strain. (2) The Katz-Wachtel phenomenon, large diphasic QRS complexes in the limb leads.

THE ELECTROCARDIOGRAPHIC DIAGNOSIS OF THE DISTURBANCES OF THE HEART'S VENOUS CIRCULATION.—LÁSZLÓ UNGHVÁRY, M.D., BUDAPEST, HUNGARY.

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CIRCULATORY CHANGES PRODUCED BY ACUTE ARTERIO-VENOUS FISTULA IN DOGS.—A. VAN LOO, M.D., GHENT, BELGIUM, AND E. C. HERINGMAN, M.D., CHICAGO, ILL.

Circulatory changes following production of a large A-V fistula by side to side anastomosis of the left superficial femoral vessels were studied in dogs anesthetized with chloralose and morphine.

Arterial pressures and pulse rate were measured with the Hamilton manometer. The immediate fall in pressure with associated reflex tachycardia upon opening of the fistula, and the rise in pressure with associated reflex bradycardia (Branham phenomenon) upon closing of the fistula were most marked within five to ten seconds. Thereafter, the values had a tendency to return somewhat closer to the control levels.

Pressures in the inferior vena cava remained unchanged. However, a definite rise in pulmonary artery pressures was noted when the fistula was opened.

These findings indicate the existence of compensatory mechanisms, which were studied by means of a Ludwig stromuhr introduced in the right femoral

artery and by measurement of the oxygen content of the venous blood from the head and the extremities. With fistula open, a definite reduction of blood flow in these areas was found.

Measurements of the asystolic arterial pressure gradient (as described by Wilkins and Schroeder) indicate that this reduction is due not only to a fall in systemic pressure but also to changes in vasomotor tone.

STUDY OF 150 CASES OF CHRONIC "COR PULMONALE".—MANUEL VAQUERO, M.D., JORGE ESPINO, M.D., BERNARDO FISHLEDER, M.D., AND NARNO DORBECKER, M.D., MEXICO, D.F., MEXICO.

In a study of 150 cases of chronic "cor pulmonale," their incidence among heart diseases was found to be 1.9 per cent and their etiological relation to pulmonary scleroemphysema was 100 per cent. The symptomatology is reviewed and the symptoms and signs, (dyspnea, cough, cyanosis, clubbing, murmurs, modifications of the second pulmonary sound, measurement of the circulation time, and so forth) evaluated, as well as their interrelationship. From the radiological viewpoint the importance of the Müller and Valsalva tests and the frequency of an opaque mediastinum (35 per cent), which approaches fibrosis in 12 per cent, a fact not mentioned before, is emphasized. From this study it is concluded that the diagnosis of chronic "cor pulmonale" may be made before evident signs of right ventricular hypertrophy appear and before heart failure ensues. In this respect, the features proposed by the New York Heart Association are useful only for the diagnosis of advanced cases of chronic "cor pulmonale"; many incipient ones pass unnoticed.

The cases of chronic "cor pulmonale" are divided into three groups, of which the first contains all of the features proposed as indispensable for the diagnosis of chronic "cor pulmonale."

I. *Incipient chronic "cor pulmonale."*—(a) Lung disease with pulmonary scleroemphysema and clinical signs of pulmonary hypertension. (b) Electrocardiographic: Slurred or broadened P wave in Leads II, III, and V_F; a P deviated to the right; diphasic P wave in V_1; presence of S_1Q_3 pattern. (c) Radiologic: normal heart contour or slight prominence of the pulmonary arch; large pulmonary branches; positive Müller and Valsalva tests. (d) Increased arm to lung circulation time. Normal lung to tongue circulation time.

II. *Evident Chronic "Cor Pulmonale".*—The following are added to the previous data: (a) Electrocardiographic: right axis deviation; small R in precordial leads; R in V_1 and V_2; deep S in V_5 and V_6; negative T wave in V_1 and V_2. (b) Radiologic: right auricular and right ventricular hypertrophy.

III. *Chronic "Cor Pulmonale" With Heart Failure.*—In addition to the previous findings, those of congestive heart failure are superimposed with the presence of fine, moist râles at the lung bases.

CLINICAL-ELECTROCARDIOGRAPHIC SYNDROME OF ACUTE OR SUB-ACUTE CORONARY OBSTRUCTION.—R. VEDOYA, M.D., AND J. GONZÁLEZ VIDELA, M.D., BUENOS AIRES, ARGENTINA.

Clinical cases of acute or subacute coronary obstruction are described which do not lead to a myocardial infarct as can be ascertained by the absence of fever, leucocytosis, or accelerated sedimentation rate.

The electrocardiographic picture is different from that observed in myocardial infarction both in appearance and evolution; its contour, however, shows great similarity to certain records obtained in patients with angina pectoris after the exercise test, as well as to the modifications induced experimentally by coronary obstruction or transitory total obstruction maintained during a shorter period than that necessary to cause necrosis of the myocardium. The electrocardiographic disturbances persist for days or weeks and the authors discuss the cause of persistence that is longer than that observed in certain experiments in the dog or in the human electrocardiogram during the effort test. The preexistant electrocardiographic picture does not allow prediction as to whether it will assume the Q_1T_1 or Q_3T_3 type when the myocardial infarct is finally developed.

Attention is called to the importance of this clinical-electrocardiographic syndrome and to the necessity of differentiating it from the classic syndrome of angina of effort and from that of myocardial infarct.

INTERAURICULAR COMMUNICATION; A STUDY OF 20 CASES.—Mario Vizcaíno, M.D., Manuel Vaquero, M.D., and Rubén Pellón Islas, M.D., Mexico, D.F., Mexico.

Twenty cases of interauricular communication, proved by cardiac catheterization (thirteen) and by post-mortem studies (seven) are presented. Thirteen are cases of the so-called "Lutembacher syndrome"; the remaining seven are isolated interauricular communications.

Clinical signs are considered significant when associated with radiologic and electrocardiographic data. These clinical signs are: systolic murmur over the pulmonary area, with or without accompanying thrill, and a loud second pulmonic sound and a palpable pulmonary closure. The systolic murmur is considered to originate in the vessel itself and not in the septal defect.

The x-ray examination shows: enlargement of the right chambers of the heart with increased pulsation, dilatation and hyperpulsation of the pulmonary artery and its branches, and a relatively small aorta with decreased pulsation. The angiocardiographic studies exhibit either simultaneous filling of all cavities at the end of the injection, or a later filling of the right auricle when the left one is just being filled, the latter being due to a left to right shunt.

The electrocardiogram, very characteristic in such cases, shows complete or incomplete right bundle branch block.

A pathognomonic sign is given by cardiac catheterization when the catheter enters the left auricle through the interauricular septal defect or, at least, when there is an appreciable difference between the mean oxygen content of the blood from the vena cava and that from the right auricle.

The pathological physiology of such a defect is discussed, the pulmonary circulation and its relation to the systemic being considered. The differential diagnosis between isolated interauricular septal defects and the so-called Lutembacher syndrome are commented upon.

THE TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS WITH PENICILLIN IN OIL AND BEESWAX.—Italo F. Volini, M.D., William S. Hoffman, M.D., and James R. Hughes, M.D., Chicago, Ill.

Eleven patients with clinical signs of subacute bacterial endocarditis, with bacteriologic confirmation in all but one, were treated with one daily dose of parenteral penicillin. Eight of these, harboring streptococci with an in vitro

sensitivity of less than 1.6 units of penicillin per milliliter, were treated with daily intramuscular injections of 2 ml. of hard Romansky formula penicillin (crystalline potassium penicillin in peanut oil and beeswax) totaling 600,000 units.

The average sensitivity of the organisms isolated in the first eight patients was 0.3954 units of penicillin per milliliter. Therapeutic blood levels proved to be adequate in all patients as compared with the sensitivity of the invading organisms. The average at two hours on single daily doses of 600,000 units was 2.27 and at twenty-four hours, 0.449 units per cubic centimeter.

The results obtained were satisfactory in eight of the eleven patients studied. There were no reactions to the many injections.

Provided the invading organisms are not too penicillin resistant, this form of therapy proved to be more satisfactory than the currently popular multiple injection or continuous intravenous routines, providing less inconvenience and discomfort to the patients and facilitating a convenient and time-saving procedure for the nursing and medical attendants.

CORONARY FLOW IN AURICULAR AND VENTRICULAR TACHYCARDIAS.—René Wégria, M.D., and Richard P. Keating, M.D., New York, N. Y.

When paroxysmal auricular tachycardia is electrically induced in anesthetized dogs, there is an immediate drop in coronary flow and mean blood pressure; then both return to their control levels. When the auricular rate is not too high, the flow may even rise above its control value. As the rate of tachycardia increases, the decrease of flow and blood pressure is more marked and more prolonged, and occasionally flow and blood pressure remain below their control values. When tachycardia stops, flow and pressure increase above control value as well as above their value during tachycardia. The higher the rate of tachycardia, the higher the increase in flow and blood pressure. Generally the blood pressure returns to normal before the flow.

In ventricular tachycardia, essentially the same phenomena are observed, with a few distinct quantitative differences, the main one being that blood pressure and coronary flow decrease more in ventricular tachycardia than in auricular tachycardia of the same rate.

The intimate mechanisms of the phenomena observed and their clinical implications are discussed.

STUDIES ON THE COMBINED EFFECTS OF CEDILANID AND QUINIDINE.—S. A. Weisman, M.D., Los Angeles, Calif.

Digitalis and quinidine are two drugs commonly used in the treatment of heart disease. Studies that confirm previous findings or offer any additional information on the action of these drugs are perhaps warranted.

The purpose of this study was to investigate: (1) The pharmacologic action of digitalis and quinidine when given consecutively at varying time intervals and when both drugs are administered together. (2) The effect of quindine on respiration.

Electrocardiographic and kymographic studies were carried out on cats. The result of this study indicates:

(1) Cedilanid and quinidine are not synergistic in their action on the heart. (2) The pharmacologic effect on the heart appears more favorable when the two drugs are given together than when Cedilanid is first given and later followed by quinidine. (3) Fatal effects occasionally attributed to the action of quinidine are perhaps frequently due to its depressent effect on the respiration rather than to its toxic effect on the heart.

It is to be emphasized that clinically it is important that quinidine be started in small doses, and that the size and frequency of the doses be gradually increased. This method may avoid some of the toxic effects attributed to the drug.

THE GRAPHIC REGISTRATION OF BASAL DIASTOLIC MURMURS.—Bertrand G. Wells, M.D., London, England, Maurice Rappaport, E.E., Boston, Mass., and Howard B. Sprague, M.D., Boston, Mass.

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THE ROLE OF IMPAIRED RENAL HEMODYNAMICS IN THE UNRESPONSIVENESS TO MERCURIAL DIURETICS OBSERVED IN SEVERE CHRONIC CONGESTIVE FAILURE.—Raymond E. Weston, M.D., Doris J. W. Escher, M.D., and Louis Leiter, M.D., New York, N. Y.

Despite the fact that many patients may respond satisfactorily to mercurial diuretics for years, the unresponsiveness to these diuretics which frequently develops in severe chronic congestive failure generally has been attributed to increased tubular resistance to mercury. The present paper is an attempt to analyze this phenomenon as a late manifestation of impaired renal hemodynamics, the importance of which in the salt retention of chronic cardiac congestive failure recently has received new emphasis.

The subjects who no longer responded satisfactorily to mercurial diuretics were all edematous cardiacs except one nonedematous hypertensive in whom a very low glomerular filtration rate was produced by the Kempner rice diet. Renal clearances of mannitol (glomerular filtration rate), para-amino hippuric acid, (renal plasma flow), sodium, and chloride were determined before and after administration of Mercuzanthin, and again, following the mercurial, when the rates of sodium and chloride filtration had been increased by the rapid intravenous administration of Aminophyllin (0.48 to 0.72 Gm.) or the continuous infusion of 4.5 per cent sodium chloride (at times, plus molar sodium lactate).

After Mercuzanthin administration, there was no significant increase in the very low later and salt excretion rates which prevailed during the control periods. However, following the Mercuzanthin, if the filtration of sodium and chloride was sufficiently increased by the aminophylline or the concentrated salt solution, there was a marked increase in urinary salt and water outputs, which, at times, approached values observed in cardiacs considered responsive to mercurials.

It is concluded that the previous failure of these patients to respond to mercurial diuretics resulted not from the usually postulated renal tubular resistance to mercury, but from the marked decrease in filtration of sodium and chloride in the presence of normal tubular function. The significance of these data will be discussed with particular emphasis on the relationships between imparied renal hemodynamics, glomerular and tubular function, and salt retention in chronic congestive failure.

ON THE POSSIBILITY OF CONSTRUCTING AN EINTHOVEN TRIANGLE FOR A GIVEN SUBJECT.—FRANK N. WILSON, M.D., J. MARION BRYANT, M.D., AND FRANKLIN D. JOHNSTON, M.D., ANN ARBOR, MICH.

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CARDIAC FUNCTION AND RECOVERY TIME.—MAX WINTERNITZ, M.D., TRUTNOV, CZECHOSLOVAKIA.

Ventricular extrasystoles due to digitalis or strophanthin are characterized by their varying electrocardiographic contour. The first tracing to be shown was obtained on a patient with mitral stenosis, strophanthin intoxication, auricular fibrillation, and bigeminal rhythm with fixed coupling. Whenever the postextrasystolic pause is shorter than 0.78 second, the next extrasystole resembles the experimental monocardiogram of one ventricle, whereas with maximal postextrasystolic pauses the next extrasystoles assume the contour of incomplete bundle branch block of the opposite type.

The second record, an instance of intermittent bigeminal rhythm, demonstrates a similar and more frequent phenomenon. Here, the actual occurrence of extrasystoles is determined by the length of the preceding pause; only the beats occurring after a long pause are followed by extrasystoles. To explain these phenomena we assume in the first case partial and in the second case complete exit block for the extrasystolic impulse.

The third electrocardiogram, an example of electrical alternans, obtained on a soldier with effort syndrome, demonstrates a different aspect of the recovery problem. At a cardiac rate up to 80 the electrocardiogram appears normal; at a rate above 120 the T wave becomes abnormal; at intermediate rates there is alternation of normal and abnormal T waves.

The last electrocardiogram, obtained on a patient with recent myocardial infarction, shows, in strict dependance upon rate, the appearance of left bundle branch block which completely obscures the evidence of myocardial infarction, present at lower rates.

THE AXIS-THEORY OF THE ELECTROCARDIOGRAM.—IMRE ZARDAY, M.D., BUDAPEST, HUNGARY.

The individual deflections of the electrocardiogram are, generally, the rectangular projections on the limb leads of the heart vector. This latter can easily be constructed if one knows the heights of the deflections in two leads. Thus, a P axis (vector) is related to auricular activity, the R axis is synchronous with the propagation of the excitation wave along the specific pathways, the S axis seems to be the expression of the spread of excitation through the muscular walls of the heart, and the T axis corresponds to the regression of the state of excitation. The physiologic basis of the Q deflection can not as yet be determined. The R axis deviates to the left both in cases of left hypertrophy and transverse heart. Differentiation between these two conditions can easily be carried out on the basis of the S axis. A similar analysis can be made concerning right axis deviation. The angle formed by the R and T axes gives evidence of myocardial disease and its site. Theoretical suppositions find corroboration in clinical data and in vectocardiography. This concept of electrocardiography permits a deeper insight into the physiologic processes underlying the individual electrocardiographic deflections.

THE U WAVE.—R. ZUCKERMANN, M.D., AND A. ESTANDÍA CANO, M.D., MEXICO, D.F., MEXICO.

The positivity of the U wave in Lead V_1 increases with the Valsalva test and decreases with the Müller test; both of these changes are evident during the initial phase. In precordial leads inversion of the U wave is observed during the ischemic phase of anterior infarcts and positivity is observed during the same phase in posterior infarcts. In esophageal leads positive U waves are seen at low ventricular levels and negative ones at low auricular levels. When septal extrasystoles are present, they are registered after the U wave and during the U-R interval (supposed septal refractory period).

These observations, together with those already postulated (that cases with unilateral increase in the ventricular pressure cause a shift of A-U toward the ventricle with lower pressure), are in accord with the hypothesis that the U wave corresponds to a delayed septal repolarization as a result of the bilateral pressure the septum is subjected to. The repolarization would take place during the phase of isometric relaxation early in diastole with its attendant fall of intraventricular pressure; the direction of the repolarization would be from the right anterosuperior to the left posterosuperior region of the septum.